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KNUD FABER

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NOSOGRAPHY
IN MODERN
INTERNAL MEDICINE

NOSOGRAPHY
IN MODERN INTERNAL MEDICINE

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WITH TWENTY-ONE FULL PAGE PORTRAITS

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PREFACE

IN THE present historical essay I have endeavored to trace one particular aspect of clinical medicine, i.e., nosography or nosology.

Clinical science is one division of pathology and this again is a part of the science of biology. The opinion expressed by Claude Bernard in 1877 still holds good: "Il n'y qu'une science biologique ou science de la vie comprenant l'état normal et l'état morbide."

The object of clinical science is the study of morbid phenomena as displayed by patients, and, within this domain, nosography—that is, the description of diseases—forms a special discipline. The importance of the nosographic method as a method in investigation has been, and is still, very differently rated by different authorities. For this reason I have considered it worth while to consider the phases through which nosography has passed and the changing judgments on its value, in order to obtain a clear idea of the importance of this method for scientific progress.

K. F.

COPENHAGEN,
September, 1919.

INTRODUCTORY NOTE

ALL THOSE whose interests are centered in the subject of internal medicine are deeply indebted to Professor Faber for so clearly tracing the historical development of this subject, and for presenting the results of his study in such a clear and interesting manner as he has done in the following pages.

In this presentation he has laid stress on the important part taken by the method of classification in the development of clinical medicine, and our respect for this method of science, which it is the fashion at present to treat almost with disdain, is thereby increased. He admits, however, that even in clinical medicine it is only one method of reaching the ultimate goal, but he also says that "to the clinician it is essential; he cannot live, speak or act without the concept of morbid categories."

Whether we agree with this latter point of view or not, all must appreciate and highly respect Professor Faber for his great sincerity and for his very able and stimulating presentation of his thesis. In this country especially, where during the past few years the subject of the proper position of the clinical branches of medicine in the university has given rise to so much discussion, this essay of Professor Faber's should be warmly welcomed. It offers abundant material to support those who are not willing to admit that clinical medicine is only an art, and it even affords some support to those who maintain that the chief object of clinicians should consist in something more than the formulation of a nosological system. One cannot read in these pages the history of the development of internal medicine without acquiring an increased respect for this branch of human knowledge and without being convinced that it will ultimately rank as a science even if, as some maintain, in its present state it does not deserve a place in that category.

Through an historical study the book attempts to formulate the idea of what clinical medicine really is, and it therefore forms a definite starting point for thought and discussion. That it will give rise to these is certain.

Moreover, besides presenting in a clear and consecutive manner the history of internal medicine, the book indicates very clearly the lines along which clinical medicine is developing today. It is, therefore, of great value even to those who are not interested in the more philosophical problems which are discussed.

Clinicians in this country are very fortunate that Professor Faber has been willing to translate this interesting paper into English for our benefit and we are indebted to the publisher for offering us this reprint of the work first published in English in *Annals of Medical History*.

I am very much pleased to have this opportunity of writing this brief Introductory Note, and to express the hope that many other English readers may receive from this book the same amount of pleasure and stimulation that it has afforded me.

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Rockefeller Institute.

NEW YORK
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PART I

Sydenham and the Nosologists

When interest in promoting medical science by independent research had been revived with the Renaissance, anatomical investigations were made the chief starting point in the quest for wider knowledge. In the beginning of the fourteenth century the practice of human dissections was begun at the Italian universities of Padua and Bologna, and with the steadily increasing number of dissections, a knowledge of anatomy was gradually gained, which reached its climax in the crowning achievements of Vesalius. Modern physiology had its beginning in Harvey's discovery of the circulation of the blood and in Malpighi's demonstration of the capillary system. Through the work of these three great men the foundations of human anatomy and physiology were laid. In pathology it proved a far more difficult and laborious task to provide a basis for a scientific structure.

In the early studies of normal anatomy some interest was exhibited in the pathological changes occurring in the viscera; Vesalius himself is even supposed to have left an important work on this subject, which has, however, been lost to posterity. Other anatomists had their eyes open, too, but what they saw remained to them disconnected observations, curiosities, and abnormalities, from which were drawn no conclusions of importance for general pathology. In this field the authority of the ancenits, of the Arabian philosophers, of Galen and Hippocrates, was still dominant, and when the first attempt at emancipation was made, the process consisted chiefly in making more or less vague deductions, based only to a slight extent on actual observation. Scientists revelled in theories and systems, more particularly in the hazy chemical theories of the Arabians, which had been disseminated among the physicians throughout Europe by Paracelsus. These theories form the earliest beginning of chemical physiology and the chemical conception of pathological phenomena.

It was not until the seventeenth century that scientific enquiry was seriously brought to bear on pathological problems, and an attempt was made to advance by means of anatomical and physiological researches.

As one of the most noted representatives of the anatomical school may be mentioned the Dane, Thomas Bartholin. He was among the first to publish large collections of pathological observations, partly reports of clinical cases and partly post-mortem findings, in his "Historiarum anatomicarum et medicarum rariorum centuriæ V et VI" and in his "Epistolæ." In his last years he planned and made studies for a large work, an "Anatomia practica" which was to contain a collection of the post-mortem findings in all organs. These studies were lost in a fire which destroyed his house, and Bonetus in his "Sepulchretum" accomplished the task which Bartholin had set himself. Bartholin, however, made only disconnected observations, and we may search his published work in vain for any general pathological points of view. A zealous but rather uncritical endeavor to collect curious cases stamped Bartholin's activity as a pathologist, and this is generally characteristic of the school he represents.

His contemporary and close acquaintance, Franciscus de le Boë, or Sylvius, at Leyden, sought, on the other hand, to construct a pathology out of the anatomical and physiological knowledge and theories of his age. Like Bartholin, Sylvius studied both normal and pathological anatomy, but first and foremost he was the representative of the iatrochemical school. He continued the work of Paracelsus and especially of van Helmont in developing chemical physiology, and he deduced his pathological system and his treatment of patients from theories in which the notion of the acid and alkaline fluids of the body, and morbid changes brought about by fermentation, played the chief part.

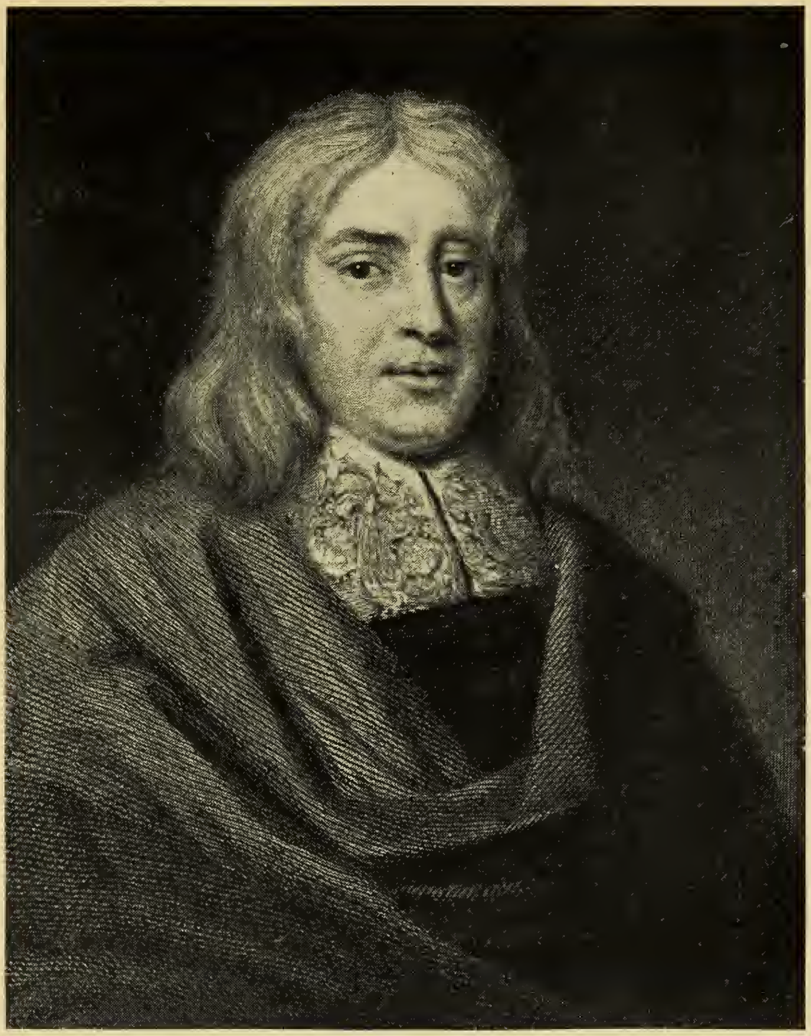
Through his assiduous activity as a teacher in Holland, to which country all learned medical men flocked, Sylvius diffused his theories throughout Europe, where his disciples further elaborated his system. In England he had a famous successor in the physician, Thomas Willis, and about the same time there also appeared a number of prominent experimentalists, as Robert Boyle, Hooke, Lower, and Mayow, who initiated the accumulation of knowledge concerning the physiology of respiration and gave further support to the iatrochemical school. It was also in England, however, during this stirring period, so significant to English intellectual life, that the man lived and worked who was the severest opponent of the speculations of the iatrochemists, and who first consciously and clearly gave clinical observation its place of honor as a scientific method—Thomas Sydenham.

In contrast with the leading pathologists on the continent, Sydenham was exclusively a clinician, and strictly confined himself to the immediate observation of pathological phenomena. He was, not without reason, the intimate friend of the philosopher, John Locke, who was but a few years his junior, and who is generally regarded as the founder of empirical philosophy; and he was an ardent admirer of his countryman, Francis Bacon. The latter, in his book on the "Advancement of Learning," had pointed out the two chief ways in which he thought medical science might be advanced. In the first place, he advised a revival of Hippocrates' old method of recording an account of the various cases, with their course towards recovery or death in order that, through such observations, the description of diseases, which had been undertaken in ancient Greek medicine but had since been quite discontinued, might be amplified and extended. In the second place he held that the pathological changes in the organs, the "footsteps of diseases" should be studied by anatomical investigations and the findings compared with the manifestations and symptoms of disease during life.

As already mentioned, medical science was fairly launched on this latter road before Bacon's time, but bedside observations were not very frequent. The various theories concerning the character and nature of diseases still formed the center of interest.

As against this, Sydenham advocated a sober observation of morbid natural phenomena, and he thus reestablished the broken connection between ancient and modern medical science. His influence was enormous, and the most interesting thing in his work is the clarity with which he set forth his method of research, only equalled in importance by the results he obtained and the advances he inaugurated. For these reasons he may be called the founder of scientific nosography.

In the introduction to the third edition of Sydenham's chief work on acute diseases which appeared in 1675, he gives an account of the principles on which his scientific activity was mainly based. His first passage



THOMAS SYDENHAM
[1624-1689]

is as follows: "After long deliberation and many years' close and faithful observation, I resolved (1) to communicate my thoughts relating to the manner of making farther advances in physic and (2) to publish a specimen of my endeavors in this way."

In his view the best manner of advancing "physic" would consist in the first place in providing a genuine and natural description or history of all diseases, a sort of natural history of disease, and in the second place, in laying down a fixed and complete method of cure for each disease. The proper description of the diseases he held to be far more difficult than generally supposed. The following principles ought to be observed:

In the first place, all diseases should be reduced to certain definite species with the same care which we see exhibited by botanists in their description of plants.

Next, all hypotheses and philosophical systems should be entirely set aside and the pathological phenomena should be described with the same accuracy that a painter observes in painting a portrait. Nothing has done so much harm as those physiological hypotheses which permit the authors to ascribe to the diseases certain symptoms which exist only in their own brains, or allow them to exaggerate certain symptoms which happen to fit in with their own theories. While referring to these symptoms, they magnify rats into elephants, they entirely neglect other symptoms which do not fit into their systems.

In the third place, in making the description, the particular and constant symptoms should be well distinguished from the accidental phenomena, which may vary with the age and constitution of the patient, or depend upon different forms of treatment.

Finally it should be observed at what season of the year the disease occurs, as some diseases follow the season as surely as many birds and plants. This is not the case with all diseases, but when it does occur, knowledge regarding this point is of great aid in determining their species and in effecting their extirpation.

Behind these principles of Sydenham's for evolving a scientific nosography there is the firm conviction of the possibility of drawing up a complete picture of each disease, a conviction which was not then current. "And, in truth," says Sydenham, "it is my opinion that the principal reason of our being yet destitute of an accurate history of diseases, proceeds from a general supposition that diseases are no more than the confused and irregular operations of disordered and debilitated nature, and consequently that it is a fruitless labor to endeavor to give a just description of them." In opposition to this point of view he insists that morbid phenomena are subject to laws. The symptoms "observed in Socrates in his illness may generally be applied to any other person afflicted with the same disease, in the same manner as the general marks of plants justly run through the same plants of every kind. Thus, for instance, whoever describes a violet exactly as to its colour, taste, smell, form, and other properties, will find the description agrees, in most particulars, with all the violets in the universe."

The scene of Sydenham's labors was unusually favorable for his observations, since the sick rate of London in his day was enormously high compared with that of modern times. One murderous epidemic succeeded another, and all the more chronic diseases flourished luxuriantly. In 1667, out of the 500,000 inhabitants of the city, some 16,000 died, while only 11,000 were born, and two years before this the plague had swept away 100,000 inhabitants. By

1667 the plague had ceased, but about 1,300 died of smallpox, 2,000 of cholera, 3,000 of phthisis, etc., and only 1,000 of old age.

Sydenham's first work dealt with the acute diseases, and by noting the course of the epidemics and the occurrence of the disease at different seasons he was aided in laying down the chief symptoms of these diseases. His description of the smallpox is a model of conciseness and has retained its worth until our day, and he made admirable descriptions of dysentery, cholera, the plague, etc. He was the first to diagnose measles and scarlatina as distinct diseases.

The task of describing the chronic diseases seemed to him far more difficult. Here he was deprived of the assistance furnished by the epidemic occurrence of the disease. It was his constant hope, however, to live long enough to provide a description of these chronic diseases as well. He had only time to give fragments, but these are of great value. Famous is his description of the gout (podagra) from which he was himself a sufferer. It was not until Sydenham described this disease that it was finally clearly differentiated from rheumatism. His description of hysteria, the psychic character of which he established, is classical; his treatises on dropsy, on syphilis, etc., are also important. He also gave the first description of St. Vitus' dance (chorea minor). Dispersed throughout his writings, we find the record of many other new and important observations. Sydenham's description of diseases is concise and lucid. We never find him quoting other authors, as is so frequently done, for instance, by Bartholin. When a young physician asked him what he should read in order to improve himself in his profession, he answered: Read "Don Quixote." So little did he respect contemporary learning. He demanded independent observation which took nothing for granted. His description of symptoms is never detailed and verbose. That his descriptions have so long been regarded as classic is because he understood so well how to point out the fundamental characters of a disease together with due consideration of its course and development. He possessed the artistic instinct of the great clinician, the power of seeing what is essential and of passing by immaterial details, and, as we have already seen, with him this was a conscious purpose, a programme, a method.

Two classes of people equally retarded the advance of medical science after Sydenham. One class consisted of those who, idle themselves, considered even the least efforts of others objectionable and excused themselves with their great respect for the old authors. To the other class belonged those who, desirous of posing as superior intellects, brought forward a wealth of arguments and speculations, quite futile when it came to curing disease. These speculative and constructive physicians were the chief butt of Sydenham's polemics, and in his views on this point he was warmly supported by his friend John Locke.

Locke had himself been trained for the medical profession and had practiced as a physician in his youth. In his work he was intimately associated with Sydenham. They visited patients together, for instance smallpox cases, and in the preface to his book on the acute diseases Sydenham expressly states that Locke fully endorsed his opinions. Among Locke's posthumous papers we have various unfinished manuscripts dating from this period of cooperation in which he further supports Sydenham's ideas. His criticism, too, was principally directed against the "chemiatrical" speculative tendency in medicine.

In his "Ars medica" (1669) he writes that he who thinks he will become an able physician by studying the doctrines of the humors, or that his knowledge of sulphur and mercury will help him in his treatment of a fever, "may as rationally believe that his cook owes his skill in roasting and boiling to his study of the elements, and that his speculations about fire and water have taught him that the same seething liquor that boils the egg hard makes the hen tender."

Sydenham had a very low opinion of the chemical school. "He blamed those who believe that medicine is to be promoted by the new chemical inventions of our day, more than by any other process whatsoever." Still he fully recognized the utility of chemistry when it came to preparing medicines. Famous are his words: "How I can make a patient vomit, and how I can purge or sweat him, are matters which a druggist's shopboy can tell me offhand. When, however, I must use one sort of medicine in preference to another, requires an informant of a different kind—a man who has no little practice in the arena of his profession." He assigned far greater importance to anatomy as a guide to the physician: "He who wants this knowledge is like a man fighting blindfold, and a mariner without a compass. Moreover, the knowledge is easily attained. Nevertheless, in all acute diseases—and two-thirds are acute—we must fairly own that there is in their nature something divine—some specific property which no speculations deduced from the contemplation of the human frame will ever be enabled to discover and exhibit." Locke made quite similar remarks in his fragment "Anatomica" dating from 1668.

Thus we see, already at the first appearance of nosography, that tendency to a divergence between clinical and analytical science on the one hand, and theoretical and deductive science on the other, which has characterized so many discussions in the past centuries and has rendered them particularly acrimonious because of the failure to distinguish sharply between the theory and practice of medicine. The theorist draws unjustifiable inferences and applies them practically, and the clinician, noting with grief all the disappointments and disasters caused by such unjustifiable and immature deductions, indignantly turns against the theorist. And if there has been any time in which an unjustifiable application of theories and speculations flourished it was during Sydenham's time. In his day there was a wide chasm between the scientific anatomical enquiries and chemical theories of the learned physicians and the doctor's practice at the bedside.

In Sydenham's writings we therefore again and again find severe polemical sallies against the speculative theorists. Sydenham was, above all, the physician, and therapeutic directions fill a very large space in his works.

He was not, however, entirely free from a speculative bias in his own therapy, though his system was simple and lucid. It started with the conception that in ague the organism, through fever, "boiled" the disease-provoking substance and discharged it with the perspiration. He adhered to the notion, inherited from the ancients, of the inherent healing power of nature, and his method of cure consisted in aiding nature with various evacuants. Attention should be called to his later doctrine of specifics, because it is so intimately connected with his whole conception of diseases as specific natural phenomena subject to particular laws. The starting point of this conception seems to have been his experiences with quinine. Quinquina had just then been brought to

Europe from Peru. Sydenham soon observed its effect in the ague and saw that it acted entirely without the assistance of the usual evacuations. Thus it had actually a specific effect in this particular disease, and henceforward it must be considered the chief task of physicians to find such specific remedies, however difficult this might seem. Sydenham himself declared that he knew of no other specific than quinine. He did not consider mercury and sarsaparilla specifics, for, although they cured syphilis, their effect was probably due only to the salivation and perspiration they promoted. Sydenham entertained no doubt that the Creator had provided specific remedies for the chief diseases, and referred to the circumstance that so few of all the many different plants had been examined for their curative effects.

After the death of Sydenham, in 1682, John Locke, in a letter to Dr. Th. Molyneux, wrote the following slightly pessimistic testimonial which gives us a good idea of Sydenham's aspirations:

> I hope the age has many who will follow his example, and by the way of accurate practical observation, which he has so happily begun, enlarge the history of diseases, and improve the

art of physic, and not, by speculative hypotheses, fill the world with useless though pleasing visions. I wonder that, after the pattern Dr. Sydenham has set them of a better way, men should return again to the romance way of physic. But I see it is easier and more natural for men to build castles in the air of their own than to survey well those that are to be found standing. Nicely to observe the history of diseases in all their changes and circumstances is a work of time, accurateness, attention and judgment, and wherein, if men through prepossession or obstinacy mistake, they may be convinced of their error by unerring nature and matter of fact, which leaves less room for the subtlety and dispute of words.

Sydenham himself regarded his work merely as an initial stage in the description of diseases. For the description of acute diseases alone "the work of centuries would not suffice," but he thought he had pointed out the right way to proceed. "I am like a grindstone," he says, "which without itself being able to cut, yet continually whets the iron."

Despite this plain indication of the road to be followed, Sydenham had no immediate successor. This was hardly due alone to that propensity in scientists to build castles in the air, to which Locke alluded, but rather to the fact that the programme laid down by Sydenham was not so easy to follow as would at first sight appear. As a matter of fact his directions concerning the method to be followed in the description of diseases were quite insufficient. They might be followed, at any rate in part, in the differentiation of various acute epidemic diseases which are characterized by occurring at different ages and at different seasons, but how should the physician be able to draw up distinct pictures from the varied mass of symptoms present in patients suffering from non-epidemic and especially from chronic diseases.

Advance might be made on some few points through unusual powers of clinical observation, such as Sydenham himself possessed, but a method rendering systematic work possible had not been found. And so we see the pathological investigators of the next century taking other courses. Leading clinicians such as Boerhaave, Hoffmann and Stahl were chiefly occupied with general pathological deductions and the framing of ingenious pathological systems. It is true that Boerhaave was a warm admirer of Sydenham and spread his fame

THOMAS BARTHOLIN
[1616-1680]

all over Europe, but he himself was rather a brilliant teacher than an independent clinical investigator, and he did not inherit the chair of de le Boë (Sylvius) at Leyden without being in some measure influenced by the chemiatric speculations of the humoropathological cast of the latter. At any rate we cannot assign any important advance in clinical knowledge to Boerhaave, however great his fame, and the same may be said in the main about his numerous pupils. But in his century a mass of material was collected through individual pathological and anatomical investigation which gradually provided a substructure for later pathological knowledge and clinical reasoning. As said before, Thomas Bartholin had already inaugurated this direction of clinical progress by his sedulous activity in collecting pathological observations, and further experience was steadily gained in the eighteenth century until Morgagni in 1760 published his great work "De sedibus et causis morborum."

There was as yet, however, no intimate connection between these anatomical observations and clinical concepts or pictures of diseases. Through the study of epidemic diseases (varicella, influenza), and of blood-poisoning (ergotism, lead-poisoning, scurvy), an ever widening knowledge of clinical medicine was attained; various nervous diseases such as sciatica (Cotugno), trigeminus neuralgia (Fothergill), paraplegia in spinal caries (Pott), angina pectoris (Heberden), etc., were described, but these additions to knowledge were made independently of the simultaneous development of theoretical knowledge and they must be looked upon as casual gleams of light rather than as the results of a methodical effort.

In the beginning of the eighteenth century, however, there was one man who attempted a direct continuation of Sydenham's nosological work and more particularly sought to carry out Sydenham's idea of describing the diseases in the same way as botanists describe plants. This was François Boissier de Sauvages, a scholar who flourished at Montpellier and published a small book, "Traité des Classes des Maladies," in 1731. He was himself a botanist besides being a physician and in his book he now sought to group the diseases in classes, orders and genera, just as natural scientists were at that time occupied in arranging plants and animals in a perspicuous system.

Such an attempt to place and group all diseases in a definite system was quite a new departure, though a few very imperfect attempts in this direction had been previously made, such as those by the Swiss physician, Felix Plater, in 1602, and the Amsterdam physician, Johnston, in 1644.

It is difficult to judge at the present time of the amount of sensation caused by Sauvages's work at the time of its appearance, but one man at least was greatly impressed by it, namely, the Swede, Carl Linné. Linné was then studying in Holland where he graduated as a doctor of medicine in 1735, the same year in which he published his "Systema naturae." From the moment of first reading Sauvages's book he became deeply interested in this man, in whom he discovered the same capacity for systematic arrangement as in himself, and for thirty years these two men carried on an extensive correspondence, became close friends, and were mutually greatly influenced by each other, although they never became personally acquainted. In 1737 Linné commenced the correspondence by requesting Sauvages to send him his book which he had "sought in vain throughout Sweden, Lapland, Norway, Denmark, Germany, Holland and

England," but which had made his mind teem with new thoughts since he had seen it at the house of a physician in Leyden. "My dull brain can only take in and comprehend that which can be conceived systematically. Any one with a bent for method will find truths in your work which will live till distant times."

In later letters he further vented his enthusiasm. "You are the only systematician among physicians, you alone have broken the ice and cleared the way. You alone have thrown open the road which the blind moles refuse to enter."

Hence, when Linné became professor of theoretical and practical medicine at Upsala, he based his lectures on Sauvages's system. After more than thirty years of work with his system Sauvages published his great main work in 1763 with the title, "Nosologia methodica sistens morborum classes, genera et species," and this work exerted a wide influence in the contemporary world. Sauvages enumerates in all 2,400 different kinds of diseases in his nosology. They are divided botanical wise into classes (10 in all), these latter again into orders (40 in all), the orders into genera (the first class alone contains 78 genera), and the genera again into species, their number, as said before, amounting to 2,400. In the preface he examines various principles for classifying diseases. A division based upon the anatomical changes would not be feasible, and still less feasible any grouping depending upon the causes of diseases, because, as a rule, the causes are quite unknown. Hence he chooses a classification based upon symptoms as the only one possible and natural. But to his mind nearly every symptom must be conceived as a separate disease, as a consequence of which he was able to enumerate the beforementioned enormous number of diseases.

Viewed with modern eyes Sauvages's system soon reveals the great shortcomings of this first attempt at a classification of morbid conditions as well as the great difficulties it involved both for the author and for the physician who was to use it. Thus no less than 18 kinds of angina are described, 19 of asthma, 20 of pleurodynia, 20 of phthisis, etc.

The grouping of the symptoms referable to the digestive organs, for instance, is specially confusing. Sauvages's seventh class comprises pains and is subdivided into five orders: The vague pains, the pains in the head, chest, abdomen and extremities. Among the 33 genera of the class we find dysphagia, cardialgia, and gastrodynia. There are 19 species of dysphagia, 6 of pyrosis, 13 of cardialgia and 20 different kinds of gastrodynia; further, under the sixth class (the debilities) occurs a genus called anorexia having 13 different species; under the third class (inflammations) we find 7 species of gastritis, and under the ninth class (the evacuating maladies) are found 12 species of nausea and 29 species of vomiting.

In reality his nosology consisted essentially in a description of symptoms, the various species of disease depending upon the various circumstances under which the symptoms appear. Such a description of symptoms was very far from Sydenham's idea of giving a proper description of the diseases. That, however, a great want had been met by Sauvages's nosology is testified by the appearance of a number of imitators and successors in the following years. In 1763 Linné published a brief "Genera morborum" for the use of his students, and in the following years extensive nosologies modelled on Sauvages's system appeared in several countries. Thus a nosol-

CARL VON LINNE
[1707-1778]

ogy by Vogel was published at Göttingen in 1764, also one by Cullen in Edinburgh in 1772, one by Macbride in Dublin in 1775, one by Sagar at Vienna in 1776, one by Vitel at Lyons in 1778, etc.

The only one of these nosologies which marked a real advance was that of Cullen. In this an extensive simplification of the system was attempted, the number of species was reduced and symptoms were grouped as far as possible into what we should now call complexes. For instance, he collected the numerous forms of anorexia, pyrosis, cardialgia, etc., under the head of dyspepsia. Nevertheless his system does not differ essentially from the others we have mentioned, his divisions, too, being based entirely on differences in symptoms.

This is also the case with the "Praxis medica systematice exposita, selectis diarii nosocomii Fridericiani illustrata" published by Bang at Copenhagen in 1789. Like Cullen's, this Danish nosology greatly simplifies matters by avoiding an undue elaboration of the individual symptoms. It was translated into German and enjoyed a wide popularity.

Although these nosologies pretended to carry out Sydenham's idea and programme by providing a description of diseases similar to that used for plants in botanical systems, yet the principles underlying all these attempts differed essentially from that recommended by Sydenham. When he described a disease he strove to characterize it by its specific course and the specific combination of symptoms exhibited. In this way he, in a manner, created new individual diseases. The nosologists of the eighteenth century, on the other hand, formed no new clinical pictures of diseases; they only catalogued and grouped the descriptions already known and left the problem of nosography at much the same point as it was in Sydenham's time.

On the whole, what difference was there between a symptom and a disease? This problem had not even been proposed, a solution much less attempted. Linné had certainly given it as his view that "symptomata se habent ad morbum ut folia et fultera ad plantam," but no attempt was made to collect the symptoms into definite units.

However, at that time methodical nosologies, such as those mentioned, were of much use and were much needed. They stimulated a more accurate description and naming of symptoms and a more secure basis was thus obtained for all discussions and clinical studies. In reality, nosologies, once attempted, have since been indispensable. It is indeed necessary to have a systematic exposition of all known "diseases," but the modern systems certainly differ in every particular from those of the past.

The earlier nosologies all exhibited a certain resemblance to Linné's system for animals and plants. Just as Linné often employed quite superficial characters in arranging his classifications, so in these nosologies symptoms having a superficial resemblance, but differing widely in pathogenesis and significance, were grouped together. During the later centuries the attempt has been made to supersede these more or less artificial systems by a more natural nosological system, by one more in accord with the nature of the phenomena concerned.

Before this problem could be successful, however, a complete revolution of clinical medicine was required. Such a revolution took place in France simultaneously with and shortly after the great political revolution during which all sciences broke away more or less from tradition and a new intellectual life began.

PART II

THE PARIS SCHOOL. ANATOMIC DIAGNOSIS

The school of medicine which flourished at Paris in the beginning of the nineteenth century is generally called the pathologico-anatomical school, as it chiefly cultivated pathological anatomy, but in reality it was a clinical school in which anatomy was always held subservient to clinical ends. Indeed, we may say that with the development of this school, clinical medicine was first raised to the dignity of an actual science.

The movement was inaugurated by two men whose scientific views exerted an exceedingly stimulating effect upon their contemporaries even though their achievements in the domain of clinical medicine itself were not of special importance. These two men were Pinel and Bichat.

Pinel in so far stood halfway in the past, as his chief work is a nosology on the pattern of the many nosologies of the eighteenth century. But Pinel's "Nosologie philosophique," which was published in

1798, differed widely from the older descriptive collections of symptoms. He laid particular stress on the importance of disregarding the individual, continually varying symptoms of disease and considering each malady as an indivisible whole taking a course subject to fixed laws. Setting aside all incidental and individual phenomena, he sought to arrive at the typical picture of the disease. In accordance with this principle he established in his system various typical "essential" fevers, each characterized by a different course and characteristic symptoms. His great personal contribution to clinical medicine, however, consists in an attempt to classify acute inflammation on a kind of anatomical basis hitherto disregarded. While in earlier times diseases were grouped on an anatomical basis as diseases of the head, chest, abdomen, etc., and of the various organs, he now divided inflammations, "les phlegmasies," into the following five orders. The diseases of (1) the skin, (2) the mucous membranes, (3) the serous membranes, (4) the connective tissue, (5) the muscles and joints. For the first time the attempt was made to demonstrate a connection and an agreement between all diseases of the mucous membranes, between those of the serous membranes, etc. He succeeded only very imperfectly in this purpose, but the idea proved fertile and was taken up by Bichat who brought it to greater perfection.

Xavier Bichat is usually, and with justice, mentioned as the man who set up the landmark between the two centuries in medicine. This young genius succeeded, in the few years of his life work, not only in completely revolutionizing anatomy and physiology by his "Anatomie générale," but also in bringing the new anatomy of the tissues to bear upon pathological anatomy and clinical medicine. He showed how each of the tissues described by him could be separately affected, and how the involvement of each tissue gives rise to different morbid symptoms. Previously, students of pathology, such as Morgagni, conceived of whole organs being diseased. Now the morbid changes in an organ were dissociated into diseases of the various tissues, each of which follows an entirely different course. The substance of the brain and its membranes may be separately affected, the various membranes of the eye have each their diseases, the bronchi, lungs and pleura likewise, and the diseases of the pericardium are different from those of the heart itself. The different tissues become diseased in the same manner quite independently of the organ to which they belong. Therefore in all inflammations there occur two groups of symptoms. One group is dependent upon the nature of the inflamed tissue, the other group is the result of disturbance in function of the organ concerned. For instance, certain symptoms, such as pain and fever, are always present and the duration and issue of the disease are much the same, whichever serous membrane is attacked, but if it is pleura that is involved, the patient will suffer from cough and respiratory difficulties; if it is the peritoneum, vomiting and obstipation are present; if the arachnoida, psychic symptoms, etc. He says in conclusion:

> Il me semble que nous sommes à une époque, ou l'anatomie pathologique doit prendre un essor nouveau. Otez certains genres de fièvres et d'affections nerveuses, tout est presque alors en pathologie du ressort de cette science. La médecine fut longtemps repoussé du sein des sciences exactes, elle aura droit de leur être associée au moins pour le diagnostic des maladies, quand on aura partout uni à la rigoureuse observation, l'examen des altéra-

tions qu'éprouvent nos organes . . . qu'est l'observation, si on ignore la, ou siège le mal?

The whole of Bichat's pathological doctrine and principle of research was exceedingly stimulating and fruitful on account of its many new points of view and suggestive starting points, and his whole personality seems to have had the same stimulating effect. There is a fire and enthusiasm in his writings which cannot fail to arouse the reader. He spent the whole of his day in the dissecting room and wrote at night, and only in this way did he accomplish so much before he died in 1802, in his thirty-first year. His example no doubt greatly influenced the many gifted young physicians who set out on their scientific careers just at this period.

Bichat's ideas found the greatest number of followers at the clinical school at the Hôtel Dieu where Corvisart eagerly cultivated pathological anatomy in connection with clinical medicine, and where the post-mortem rooms were daily visited by the young students, Bayle and Laënnec.

Corvisart has laid down his principles of research in the introduction to the "Essai sur les maladies et les lésions organiques du coeur et des gros vaisseaux" which appeared in 1806.

With Corvisart the old era of systematic nosology comes to an end. After this, medical progress no longer depends merely on grouping the symptoms of disease. In order to increase existing knowledge concerning the real nature of disease Corvisart laid stress upon the study of the pathological changes in the organs. Such studies had been prosecuted since the Renaissance and had resulted in Morgagni's famed book, "but," he says, "this fine work has served more to adorn the works of other physicians than to advance the art of recognizing the organic diseases. It should not be our object to search, out of a barren curiosity, for what the corpses may offer in the way of remarkable things, but to recognize the diseases by definite signs and constantly recurring symptoms." He therefore thought that the problem might be formulated in much the same way as Morgagni formulated it in the title of his book, but conversely. Morgagni had called his work, "De sedibus et causis morborum per signa diagnostica investigatis et per anatomen confirmatis," but added Corvisart, "it would require no less than a second Morgagni to produce such a work." The whole programme of the new school is contained in the above sentence, and there was really no lack of men who were Morgagni's equals. Corvisart himself made a beginning in his book already mentioned, which deals with the general symptomatology of heart diseases from this point of view. In this book he gives a classical description of cardiac dyspnea. He adopted the "Inventum novum" published by Auenbrügger in 1761, *i.e.*, direct percussion, in order to demonstrate hypertrophy of the heart, and he sought to correct his diagnoses through succeeding post-mortem examinations. But all this was only the beginning.

The genius who really broke new ground was Laënnec, whose "Traité de l'auscultation médiate" belongs among the works which have marked an epoch in medicine and more particularly in internal clinical medicine.

It is now just one hundred years since this book saw the light, and from the time of its appearance the physician saw his task at the bedside change. The physician began now not only to observe, but to examine the patient. Laënnec's work produced also a revolution in nosography, a revolution in the manner of describing and classing the morbid phenomena.

RENE-THEOPHILE-HYACINTHE-LAENNEC
[1787-1826]

In his preface to the 2nd edition of his book (1826) Laënnec describes his method in the following words:

> Le but que je me suis constamment proposé dans mes études et recherches a été la solution des trois problêmes suivants:
>
> 1. Distinguer sur le cadavre un cas pathologique, aux caractères physiques que présente l'altération des organes;
> 2. Le reconnaître sur le vivant, á des signes certains, et autant que possible physiques et indépendant des symptomes, c'est-à-dire du trouble variable des actions vitales qui l'accompagnent;
> 3. Combattre la maladie par les moyens que l'expérience a montré être les plus efficaces: en un mot, j'ai tâché de mettre, sous le rapport du diagnostic, les lésions organiques internes sur la même ligne que les maladies chirurgicales.

As will be seen, his scientific programme coincides very nearly with that of his teacher, Corvisart. He carried on pathologico-anatomical investigations, but constantly had in mind the utility of pathological anatomy for clinical medicine. "C'est le flambeau de la nosologie," he exclaims in 1812, greatly preferring the anatomical to the etiological or symptomatic method for distinguishing the various diseases, because he believed the anatomical characters to be the most constant and the easiest to recognize.

But when it came to recognizing in the living patients the anatomical changes found in the dead, there was still far to go. It was while considering this that he made the greatest advance when, in 1816, he conceived the idea of indirect auscultation, and this resulted in the invention of the stethoscope. By auscultation he was able to demonstrate the signs of morbid changes in the organs much more perfectly than he could by percussion alone, and the subjective symptoms, therefore, became of secondary importance.

After having described and classified all the phenomena observed by means of his stethoscope, he explained in his "Traité de l'auscultation médiate" the anatomical changes in the lungs corresponding to the stethoscopic phenomena, basing his explanations upon post-mortem findings. Before Laënnec's time a physician's examination of his patient consisted entirely in observing his appearance, feeling his pulse, looking at his tongue, examining the urine and the like. Now a really objective examination of certain organs could be made, at any rate, of the organs of the thorax. Objective criteria were henceforth demanded, and nosography had thus been placed on quite a new and firmer footing. Laënnec caused the germs provided by Pinel's and Bichat's anatomical ideas to spring into life in clinical medicine.

By comparing the conditions present in the patient with the course of the disease and the lesions found at post-mortem examinations Laënnec created a series of entirely new and classical pictures of disease. Thus he was the first to describe emphysema, acute and chronic edema of the lungs, bronchiectasis and gangrene of the lungs. He further described pneumothorax, and he distinguished pneumonia from the various kinds of bronchitis and from pleuritis. Before his time physicians had not been able to distinguish between these various affections, but merged them all under the term peri-pneumonia which had been inherited from the ancients. Having made these distinctions he was able to give a clinical and anatomical description of pneumonia which holds good to this day.

His greatest accomplishment, however, was his description of tuberculosis. It may be said that he was the first to establish the conception of tuberculosis as a morbid unity. Phthisis was, of course, known from the time of the ancients. The advanced stage with consumption, the expectoration of pus or blood, fever and diarrhea, had been known and described, but a number of other chronic lung diseases such as bronchitis, empyema, gangrene of the lungs, etc., were confused with phthisis, and the early stages of the disease were little known. On purely symptomatic grounds various kinds of consumption had been demonstrated, as many as twenty varieties by Sauvages, fourteen by Pascal, etc. Anatomical tubercles were known since the time of Sylvius and Morton, and the conception had gradually gained ground that tubercles possessed a certain significance in the development of phthisis. Laënnec's contemporary, Bayle, got so far in simplification of the problem as to describe only six different kinds of phthisis. Laënnec was, however, the first to recognize that all these varieties were but stages in one disease, tuberculosis, and to show how to distinguish it from similar morbid states. Moreover, he showed that miliary tubercles, the larger yellow tubercles and the grey and yellow infiltration are all but different stages of the same process. Clinically he demonstrated that the process usually begins in the apex of the lung, and that the various anatomical changes may be demonstrated by means of stethoscopy, and finally he conceived and described tuberculosis of the lungs as a special disease differing from all other disease processes. He also recognized that tuberculosis in other organs and also scrofula were varieties of the same general disease.

Laënnec died in 1821, only forty-five years old, but a number of clinicians carried on the work in accordance with the programme laid down by Corvisart and by him. In all fields of internal clinical medicine there was a regeneration, and a nosography was created of hitherto unknown comprehensiveness and certitude. The most prominent names of this French school are G. L. Bayle, Andral, Louis, Bretonneau, A. L. Bayle, Bouillaud, Cruveilhier, Chomel, Alibert, Rayer, and Piorry. Their works and influence have so often been described that we may here content ourselves with a brief mention. With regard to them all, it holds good that it was the careful examination of the patients and the exact post-mortem examinations which led to the advances in knowledge which they made and to their continual discovery of new diseases, or rather, to the continual establishment of new categories of disease, all of which had a pathologico-anatomical basis, and had clinical features characterizing them as well-marked individual diseases. As typical examples of their work may be mentioned Bretonneau's description of diphtheria, Louis' and Andral's studies on typhoid fever, A. L. Bayle's discovery of dementia paretica, Cruveilhier's discovery of chronic ulcer of the stomach, Bouillaud's establishment of mitral insufficiency and of rheumatic endocarditis.

Bacon's sentence *ars medica tota in observationibus* which Laënnec had employed as a motto, became a guide to the school.

The importance of hospital facilities for making these careful observations at the bedside and at the post-mortem tables caused hospital work suddenly to gain a significance which it had never had before. It was only in the wards of the hospitals that the careful examination of patients which was now required could take place; it was in the post-mortem rooms that Bichat and Laënnec had carried on their anatomical studies.

It was the results of such careful examinations of patients and just as careful post-

PIERRE-CHARLES-ALEXANDRE LOUIS
[1787-1872]

mortem observations which were collected by Andral in 1823 in his classic "Clinique Médicale" which became the model for all works on clinical nosography during the following decades. The mode of exposition which he employed in this work was unusually lucid and methodical. In discussing each disease he first describes a series of cases ending fatally and describes the anatomical findings, then he describes a series of cases terminating in recovery, and finally he collects the anatomical as well as the clinical findings, and draws a picture of the disease in its entire course and in its different phases.

The same method was followed by Louis who gradually became the leader of the Paris school. For eight years he gave up all private practice, spent four or five hours daily at the hospital and gave at least two hours to every post-mortem examination.

His first work on tuberculosis of the lungs was based on 167 clinical cases of pulmonary tuberculosis with autopsy examinations, his work on typhoid fever on 138 cases with dissections. In the prefaces to his works in which, like most of the authors of this period, he diffusely discussed his principles of research, he emphasized how important it is for the physician to question his patients carefully, ascertaining what symptoms were present, and lacking these, being careful not to exert any suggestive influence on the patient while taking the history. The next step should consist in determining whether the organ to which the symptoms are referable, as indicated by the disturbances in function, shows lesions at the post-mortem examination that satisfactorily explain the symptoms. In this the greatest objectivity should be observed. And as a motto for his work on typhoid fever he cites Rousseau's familiar words from "Émile": "Je sais, que la vérité est dans les choses et non dans mon esprit qui les juge, et que moins je mets du mien dans les jugements que j'en porte plus je suis sûr d'approcher de la vérité."

As may be inferred from this quotation he was methodical rather than ingenious. He was almost pedantically exact and can hardly be called an innovator. He therefore gradually invested the school with a certain tendency to dryness, giving more and more weight to a numerical registration of morbid phenomena. He introduced the statistical, numerical method into clinical research, but in a certain degree this occurred at the cost of direct biological observation.

On this point he was in marked contrast with another of the most prominent members of the school, Bretonneau. This remarkable and gifted clinician spent his life as a hospital physician at Tours. Very fertile in original ideas with which he orally enriched his pupils, he seems to have been indisposed to commit them to paper. He has in fact left behind him only one larger work, his book on diphtheria, which appeared in 1826. It may be said that the scientific history of diphtheria began with Bretonneau, since he was the first to write diphtherial angina and croup into an etiological and clinical entity. His second great subject of investigation was typhoid fever in which he demonstrated the intestinal lesions, and he therefore named this disease "Dothiénentérie." In 1826 Bretonneau's disciple, Trousseau, gave an exposition of the latter's ideas and observations concerning dothiénentérie, and Bretonneau's own great work on this subject seemed to be nearing its completion when Louis and Andral in 1829 brought forward their works on typhoid fever and thus rendered Bretonneau's book unnecessary, or at any rate, deprived him of the desire of finishing it.

Our own special interest in Bretonneau is excited chiefly by his general points of view concerning specific inflammations and specific diseases. According to Bretonneau it is the specificity of the inflammation much more than its intensity or seat in the various tissues which influences the morbid phenomena: "C'est à la spécificité de l'enflammation, que se rapportent la durée, la gravité et le danger de la plupart des pyréxies." He states that all tissues seem liable to be affected by various kinds of inflammations, but the inflammations of the skin offer the greatest variety; the mucous membranes, however, may also be the seat of different kinds of inflammation.

As an example of a specific inflammation he refers to the membranaceous diphtheretic inflammation of the throat; in typhoid fever there occurs another variety in which a kind of pustulous exanthema occurs in the mucous membranes of the intestine, just as in smallpox a special type of exanthema is present on the skin. It is upon the demonstration of the specific character of

GABRIEL ANDRAL
[1797-1876]

a disease that diagnosis, prognosis and treatment depend. Since Bretonneau, the specificity of diseases has in fact always been implied; this is shown by the different names given to the cutaneous inflammations, "even the physicians who refuse to accept it because it is opposed to their theories, defer to it in practice."

Of special interest is the manner in which Bretonneau sought to give experimental support to his theory of specificity. By application of the extract of cantharides he succeeded in producing a membranous inflammation in the mouth and throat or in the conjunctiva of dogs. The appearance of the lesion was exactly similar to that of real diphtheria, but the course of the disease was quite different, the process was localized, extremely benign, and was not accompanied by fever or other general manifestations. "Ce quelque chose de spécial, ce 'quid divinum,' qui ne peut être saisi, et qui, de l'aveu d'Hippocrate, échappe à toute explication" was wanting. Like Sydenham he stops at this "quid divinum," this mysterious factor which determines the course of a disease, its specificity.

Bretonneau had not the same influence on his contemporaries as Louis, and, under the leadership of the latter, purely anatomical diagnosis became more and more dominant, but it will be easily seen that the points of view and attitude of mind revealed by Bretonneau in his writings indicate that in him a further and considerable development of Laënnec's ideas concerning nosography, had taken place. The French physicians of this period were constantly engaged in isolating and describing new types of disease, and this aided greatly in maintaining and developing Laënnec's ideas.

It must not, however, be understood that there were no difficulties to be overcome. On the contrary, the new school met with keen opposition, and Laënnec and Louis, especially, found a bitter adversary in the somewhat fanciful Broussais, who was, however, a gifted agitator. Their controversies played a great part at Paris in the first part of the century and finally ended in the defeat of Broussais. Nevertheless, it is not unimportant to draw attention to some of the views which he advocated, because they represent certain principles in clinical research which have retained a certain vitality, especially in Germany.

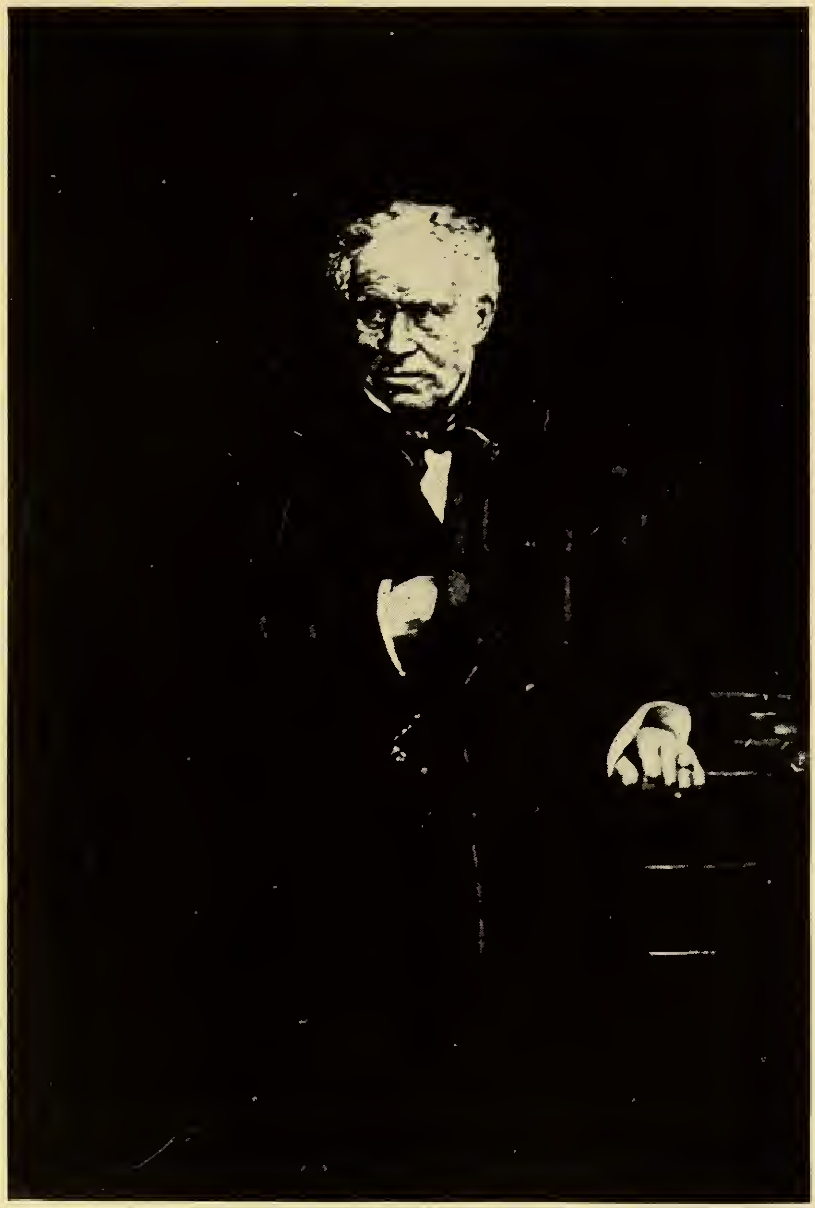
Broussais called his doctrine "physiological medicine" because he wished to attach more weight to the functional disorders of the diseased organs than to their anatomical alterations. He was the disciple of Bichat in so far as he sought to locate the diseases in the separate organs, but he opposed the tendency of the modern school to draw up definite clinical pictures of disease ascribing to each disease a typical course and sufficiently well-marked characteristics as to justify its designation as a distinct entity.

He maintained that symptoms are subject to no law, but combine in ever varying groups, no two cases being ever found alike. It was, therefore, necessary to investigate closely the physiological conditions present in each separate case. It was unjustifiable to regard tuberculosis as a morbid entity. Viewed anatomically, tuberculosis was only a chronic inflammation of the lungs, a chronic pneumonia, without particular characters. Inflammation, wherever occurring, was due to a diminished or increased degree of that "irritation" which was, to him, the vital principle. According to Broussais, the practice of the pathologico-anatomical school of setting up diseases was in fact only the continuation of the infelicitous idea of the older nosologists of conceiving of diseases as special beings like plants. This was "ontology," and it was chiefly this and the accompanying "fatalistic" conception of the course of the diseases which he persecuted with all his hate and scorn.

Those groups of symptoms which are given out as diseases are metaphysical abstractions which by no means represent a constant unchangeable morbid condition, and which we cannot be certain of finding in nature. They are factitious entities (*entités factices*), and all those who study medicine according to this method are *ontologists.*

To regard the succession of symptoms observed as the necessary and unchangeable course of a disease, means the creation of a factitious entity, means the making of ontology.

Broussais in a way hits the very center of the mark in his criticism of the aims of the Paris school, since in all the coryphés of the school, from Pinel with his essential fevers, to Laënnec with tuberculosis and Bretonneau with the specific maladies of the mucous membranes, we meet with this tendency to set up "factitious entities," typical diseases, and these aims are diamet-



PIERRE BRETONNEAU
[1771-1862]

rically opposed to Broussais' physiological medicine which fanatically opposes everything specific. It is the same antagonism which we found between the men of the chemiatrical school on the one hand and Sydenham and Locke on the other, and in one shape or another we shall meet it again during the whole of the nineteenth century.

Broussais was of course right in his argument that all entities of disease are abstract concepts created by the human brain, but he did not see that the same holds true of all species, even of botanical and zoological species, though Broussais drew a contrast between these and what he called the "factitious" entities in medicine. Even after the zoological species have been deprived of their Platonic divineness, they are still as necessary as before in biology, and an analogous situation exists in respect to diseases in medicine. It is only when we forget that species is a concept derived from individual observations, and assign to it an absolute value, that we can be dubbed ontologists.

The habit of regarding diseases as entities, as a kind of beings, forced itself on the clinicians with irresistible power from Sydenham to Bretonneau. This gave support to the criticism that there was a complete failure to recognize the essential principle in the delimitation of a given pathological species from other pathological conditions.

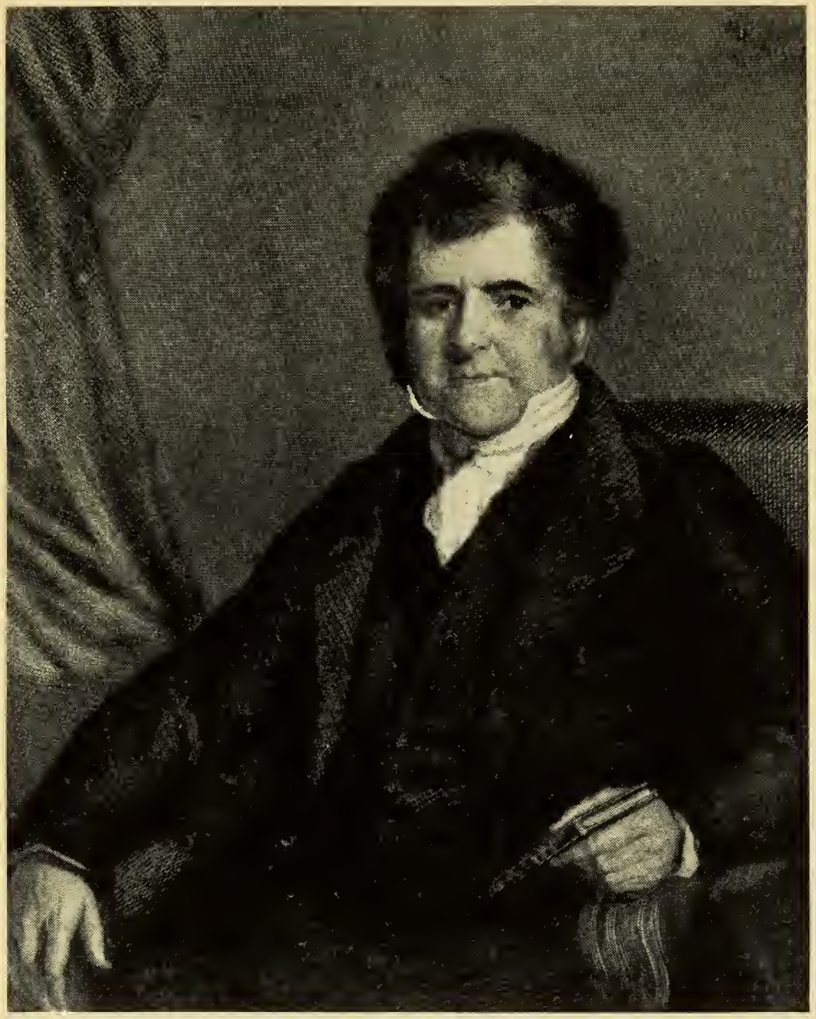
Although anatomical changes were considered of great importance by the men of Laënnec's school, these men were too much clinicians to rely on them alone in classifying diseases. They understood that there existed laws relating to the combination and course of symptoms which could not be neglected. As previously mentioned, suggestions appeared in the works of Bretonneau as to methods for solving the problem, and his suggestions were extremely fruitful in later times.

The clinical scientific movement spread quickly from Paris to other countries. From all parts of the world young physicians flocked to Paris in order to learn the art of stethoscopy as well as anatomical diagnosis, and centers of learning arose in which the new teaching was not only applied in the practice of diagnosis, but also in which the principles of research actuating the Paris school were employed in further independent investigations along similar lines.

The first place in which such a clinical school arose was Dublin. About 1820 Ireland was beginning to recover from a series of violent and disastrous social and political shocks, and about this time the physicians of Dublin found a leader in Robert Graves. After pursuing his studies on the continent for several years, Graves had been appointed chief physician to the small Meath hospital, and here also shortly afterwards William Stokes obtained a post. These two eminent clinicians form the center of a group of physicians whose names are still familiar on account of the clinical discoveries with which they were associated. Among these physicians were Cheyne, Adams, Corrigan, and others. These clinicians are now chiefly remembered as having described the "new" diseases or complexes of symptoms with which their names are associated, as, for example, Graves' disease, Adams-Stokes' disease, Cheyne-Stokes' respiration, Corrigan's disease, etc.

Almost simultaneously new clinical schools appeared in London, that at St. George's Hospital, where Hope worked, and the school of Guy's Hospital being of special importance. At the latter school Thomas Addison and Richard Bright were the leaders and they became the most noted of the "great men of Guy's," among whom was also Hodgkin. In Bright's "Reports of Medical Cases," published in 1827, he showed for the first time the connection between anatomical changes in the kidneys and dropsy, and albuminuria, and thus created the clinical picture of that chronic inflammation of the kidneys which still bears his name, and the nosography of which he further elaborated in his later works. The names of Addison and Hodgkin also became attached to definite diseases, and the same is true of the names of other physicians who were then practicing in London and Edinburgh, such as Parkinson, Abercrombie and others.

All these English clinicians worked according to the same principles as those that guided the Paris school, and their chief contributions were to nosography. It was the combination of anatomical and clinical investigation which led to the results which they obtained, and they held the opinion, perhaps even more strongly than the French physicians, that pathological anatomy was merely an aid to clinical medicine and must always be subordinated to the latter. We find this clearly expressed by Graves in his famous clinical lectures:



RICHARD BRIGHT
[1789-1858]

In order justly to estimate the importance of morbid anatomy, we should recollect that the first alteration in the picture of a part is not the cause but the consequence of disease. . . . Thus the physical alterations which attend external inflammation, the tumefaction, the heat, the redness are not the causes but the consequences of disease. But in thus reducing them to the rank of symptoms, do we diminish their importance? Certainly not. For being immediately connected, as effects, *with* the primary cause, they prove the most useful of all symptoms, in enabling us to ascertain the seat and progress of diseased action.

Graves, of course, fully acknowledged the importance of Laënnec's anatomical diagnosis, but he held the conception of "disease" as of primary significance and was therefore in harmony with Sydenham's and Bretonneau's doctrine of the specificity of disease.

Thus the French and English clinicians became co-workers, starting with very similar points of view, and as a result, an entirely new clinical medicine developed during the first part of the nineteenth century. A series of new diseases was described and these were made easy to recognize by the discovery of "pathognomonic" symptoms and characteristic objective signs. The course and whole characteristic picture of these diseases were definitely outlined. The violence with which clinical medicine was completely revolutionized in the course of a few decades by these important and striking discoveries will always remain one of the wonders of medical history.

The stir of this scientific movement spread quickly to other countries. In America the brilliant pupil of Louis, W. W. Gerhard, besides other accomplishments, described tubercular meningitis in children, and he was also the first clearly to differentiate typhus and typhoid fevers. In Denmark, Seligman Trier, head physician at Frederiks Hospital in Copenhagen, introduced stethoscopy as a diagnostic method into Scandinavia, and in 1830 published a book of "Directions in the Art of Stethoscopy." Scientific work in this field was not continued in Scandinavia, however, and only later, through the efforts of C. E. Fenger, who demonstrated "the echo in the human lungs," were the French ideas, more particularly Louis' statistical method, adopted in this country.

The first place in the Germanic world in which to any extent Corvisart's and

Laënnec's and other exact methods of physical examination were adopted, was Vienna. Here Auenbrügger had formerly developed the method of percussion, and here now the clinician, Skoda, and the pathologist, Rokitansky, became the leaders of the "new school of Vienna."

They followed largely along the lines laid down by the Paris school. Rokitansky, drawing on an immense body of material, most industriously and systematically continued the study of the pathologico-anatomical changes in the organs which had been undertaken by the French pathological anatomists, while Skoda extended and developed Laënnec's stethoscopy. By intimate cooperation these two scientists greatly advanced the art of anatomical diagnosis, and the Allgemeines Krankenhaus of Vienna was long a gathering-place for young physicians.

There was, however, an essential difference between the French and Vienna clinical schools. In Skoda's chief work on percussion and auscultation which appeared in 1839, there is much criticism of Laënnec's views, particularly of his views concerning the significance of certain signs. Laënnec had attempted to characterize the various diseases by definite stethoscopic findings, and had, for instance, pronounced crepitation "pathognomonic" of pneumonia. Skoda was opposed to this view. Skoda attempted to explain the phenomena observed by percussion and auscultation by purely physical laws and he employed the methods of auscultation and percussion to demonstrate anatomical changes in the lungs, but he would hear of no definite diseases or pathognomonic signs of such. In these views he accorded with Rokitansky, and like him, placed anatomical alterations first in the classification of morbid processes, and held that the task of clinical medicine was confined to demonstrating these anatomical changes in patients. He thus entirely subordinated clinical medicine to pathological anatomy and made anatomical diagnosis in the literal sense of the word the end and object of his efforts. As a matter of fact, Laënnec, too, had seen quite clearly that only certain purely physical changes in the lungs could be demonstrated by auscultation, but he utilized the findings as part of the morbid picture and described, for instance, a typical stethoscopic finding in pneumonia as a characteristic feature of that disease. Skoda raised strong objections to this, and he seems to have lost the power of seeing precisely what was clinically typical in proportion as he became absorbed in the study of the physical laws underlying the percussive and auscultatory phenomena. Indeed, he quite deferred to Rokitansky who, in his textbook of 1846, drew the oft-cited conclusion "that pathological anatomy should be the base not only of the knowledge of physicians but also of their practice, as it contains all there is in medicine of positive knowledge and the foundation of it!" With such views scientists had wandered far from the nosography of the English and French, and landed in anatomical diagnosis of the purest and dryest sort. Is it to be wondered that it brought with it a complete therapeutic nihilism in internal medicine?

At Berlin it was Schönlein who had the merit of introducing Laënnec's diagnostic methods. Through his vigorous personality he greatly influenced the younger generation of physicians, though as a scientific worker he was not very productive. In his earlier years he was greatly influenced by German "Naturphilosophie," and by the earlier clinicians of the eighteenth century, and he also became engrossed in devising nosological systems. The systems originated by him and his disciples (Eisenmann, Fuchs and others) had a strong philosophical character and were of no lasting value. Only when he came to La Charité at Berlin in 1839 and at the same time adopted the French methods of physical diagnosis did he grow to be the highly valued teacher of the rising generation in the medical world.

PART III

GERMAN PHYSIOLOGICAL MEDICINE

While the new school of Vienna was developing clinical medicine on pathologico-anatomical lines, another tendency began to assert itself in Germany. This was manifested by a disregard of the nosography of the Paris school, accompanied by an effort to reconstruct clinical medicine on physiological lines.

This movement had indeed already been initiated in France by the experimental physiologist, Magendie. In his lectures of 1836 on the "Phénomènes physiques de la vie," he discussed the problem both from the physiological and the pathological standpoint and published his own views concerning the best methods to be employed in increasing knowledge concerning morbid phenomena. He admitted no essential difference between physiology and pathology; they appeared to him as one science; pathological phenomena are only modified physiological phenomena. "La médecine n'est que la physiologie de l'homme malade." Both sciences should, therefore, be studied by the same exact methods. Through pathological anatomy alone complete knowledge concerning disease could never be acquired. The changes found in the organs after death cannot explain all the phenomena observed before death, and the local lesion is, as a rule, only the outcome of an action on the economy of the whole system.

In Germany it was chiefly the physiologist, Joh. Müller, who advocated similar views, and his disciples carried on the movement with vigor. As a physiologist he continued the work begun by Magendie, but his influence extended far beyond physiology on account of the consistency with which he demanded exactness and conciseness, not only in physiology, but also in pathology, and his importance for German medical science may best be conveyed by mentioning some of the men who counted themselves his disciples, such as Schwann, Remak, Wunderlich, Henle, Traube, Virchow, Helmholtz, Kölliker, DuBois-Reymond, Brücke and many others.

In the beginning of the forties some of these enthusiastic young physicians set high the banner of science in medicine. Almost simultaneously three periodicals were started as organs for the new school. In 1842 Wunderlich and Roser began the publication of the *Archiv für physiologische Heilkunde* at Würzburg and in 1847 Henle at Zürich established the *Zeitschrift für rationelle Medizin.* At Berlin Ludwig Traube in 1846 began the publication of his *Beiträge zur experimentellen Pathologie und Physiologie*, which, in its first numbers, contained his own well-known investigations on the consequences of cutting the vagus nerves and the pathogenesis of the resulting pneumonias (*Schluckpneumonien*), and Virchow's still more famous work on embolism and thrombosis. These *Beiträge* only appeared for one year, however, as they were superseded by the famous *Archiv für pathologische Anatomie und pathologische Physiologie und für klinische Medizin* which was founded by Virchow and Reinhardt in 1847.

Even if these three journals differed somewhat in character they all sounded the same note, demanding a really scientific treatment of the problems in medicine, based on experience and experiment. The description of phenomena was no longer sufficient; an attempt should be made to understand their interrelation, their genesis and development, and the principle first enunciated by Magendie, that pathology is the physiology of the diseased individual, was constantly emphasized.

The scientific life which now unfolded itself was all the more effective because prior to this there had been an absolutely barren period for medicine in Germany. German science was greatly under the influence of "Naturphilosophie" at the beginning of the nineteenth century. Medical science was dominated by Schelling's philosophy and a priori deductions and superficial analogies replaced scientific observation.

From Jena, the home of romanticism, had issued the so-called "school of natural history" in medicine, as it was named by K. W. Stark. He has related, more or less vaguely, certain notions held by this school, such as that diseases should be regarded as parasites, not as produced by parasites, but as being themselves a kind of parasite existing on the sound organism in which they develop. The diseased organ is to be considered not only as a degenerated part of the body, but is itself a special organism with its own laws of development, a kind of parasite. The difference between the cause of the disease and the disease itself was overlooked, and thus an "ontology" of a much more stalwart character than had hitherto been known was established.

By some of the disciples of this school these notions were carried to the verge of the grotesque. Thus Karl R. Hoffmann, influenced by certain ideas in Schelling's "Naturphilosophie," described in his "ideal pathology" the various morbid conditions as a kind of retrogression to lower grades of evolution. Rachitis signified a return to the mollusca because the bones became soft. He thought individuals suffering from certain digestive disorders had descended to the rank of cattle. That the tongue got white, the urine sedimented and eructation and vomiting occurred, all indicated a tendency to rumination. A finer example of "false analogies" can hardly be adduced.

In the face of such unscientific views, the new movement had the effect of a revolution, and the two "Swabian reformers," Wunderlich and Roser, who were the first in the arena, created an enormous sensation in the medical world.

The title which Wunderlich had given to his *Archiv* led to the name "physiological medicine" soon becoming accepted as the name of the school. In his "Geschichte der

Medizin," published in 1869, Wunderlich says that this name was chosen "on the one hand to express the fact that pathology, in contrast to all ontological and personifying conceptions, is only the physiology of diseased man, on the other hand, to call to mind the fact that pathology requires the same means and methods to establish facts, and the same logic in argumentation, as were already recognized in the science of healthy man." We thus see that the selection of the name "physiological medicine" had a double significance. From the very beginning there existed the intention to replace anatomical research entirely by physiological investigation, to pass from the purely descriptive method to a consideration of the relations existing between various morbid phenomena, and to establish a pathological physiology such as had been suggested by Hunter, Dupuytren and Magendie. But in addition there was also the firm resolve to abandon the "ontology" of earlier times, above all as it displayed itself in the German school of natural history with its almost personifying conception of diseases. This attitude, however, involved a strongly antagonistic position towards the whole doctrine of the French pathologico-anatomical school which Broussais, as we have seen, had declared to be a dangerous ontology. On the whole Broussais and Magendie were cultivated and commended at the cost of Louis and his fellows, and Bretonneau's views were entirely disregarded.

On reading the introductory articles containing the programmes of the above-mentioned periodicals we receive a vivid impression of the excessive enthusiasm with which German medicine, after long languishment, woke to the vigorous activity which was soon to give it a leading position in the world, a leadership to be retained under the guidance of Virchow during the remainder of the century. But from these same articles we also receive the impression that there prevailed extremely narrow and limited views concerning clinical medicine, and we can also detect the germs of these opinions which were soon to lead German medicine astray on certain important points.

As already said, the members of this school from the very beginning resisted every endeavor to establish definite clinical pictures, or to describe individual diseases, and all mention of specific characters was opposed and dubbed ontology, or characterized as a relic of an unscientific and antiquated age.

Some passages from Wunderlich's introductory article to the first number of *Archiv für physiologische Heilkunde* are of interest in this connection:

> Such a view which takes abstract concepts for things, implying their actual existence and at once treating them as entities, is called ontology. Frequently as has this logical blunder crept into medicine and flourished there, after Broussais' time it will hardly be heard of again.
>
> To the most widespread and the most dangerous consequences of ontology belongs the practice of setting up species of diseases which have been grouped in classes in the same way as plants. By raising them to the dignity of species these ontological personifications received, as it were, the sanction of natural history.
>
> The phenomenologist certainly uses such clinical pictures as dysentery, cholera, scrofula, but he only assigns importance to them as a practical make-shift borrowed from the popular, unscientific view of things. He knows that such a group is no definite physiological whole, no organic entity. He knows that it is an impossibility to decide, or is at any rate quite an arbitrary decision, where the limit is to be drawn between dysentery and enteric diarrhea,

LUDWIG TRAUBE
[1818-1876]

> between rheumatism and arthritis. But to the ontologist the assumed disease is a dogma; the group once collected, it becomes a concept, an entity. Thus these model pictures of diseases arise, which contain no essential mark, no mark which may ever be missed—this compendium of diseases to which we only exceptionally, or by using compulsion, find parallels in nature.

Here we see how entirely he dissociates himself from the French clinical school, and we find similar pronouncements by the other representatives of German physiological and rational medicine in the forties.

For instance, we find quite a similar line of thought expressed by Traube in his *Beiträge* and by Virchow in the articles sketching his programme in the first numbers of his *Archiv*. In the preface to his periodical Traube states that there was only one means of escaping from the uncertainty and confusion which prevailed in pathology, only "experimentation combined with observation can make pathology what it should be, an exact science."

Virchow's views of clinical research are found expressed in the prospectus contained in the first volume of his *Archiv* (1847):

> The ideal we shall strive to realize, as far as it is in our power, is, that practical medicine

shall become applied theoretical medicine, and theoretical medicine shall become pathological physiology. Pathological anatomy and clinical medicine, the justness and independence of which we fully recognize, are essential to us as sources of new questions, the answering of which will fall to pathological physiology.

In a following article "Über die Standpunkte in der wissenschaftlichen Medizin" he continues:

> Pathological physiology takes its questions partly from pathological anatomy, partly from practical medicine; it creates its answers partly from observations at the bedside, and thus it is a part of clinical medicine, and partly from experiments on animals. The experiment is the ultimate and highest resort in pathological physiology.

Like Wunderlich he repudiated all ontology, all talk of specific diseases and associated specific therapy. In the next number of the *Archiv* he continues:

> Indeed therapy knows only too well the giant whose far-reaching shadow has withered so many fresh shoots in all the provinces of medicine and made so many pleasant flowers fade before their time. It is *ontology* which has inflicted wounds of no less depth in pathological microscopy than in therapy and diagnosis.

Consider only how much toil it has cost and still costs to conquer ontology in the so-called physical examination of the thoracic organs, and keep fresh in the consciousness of physicians the fact that we are able to recognize only the consolidation of the parenchyma of the lung and the contents of the bronchi but not immediately the pneumonia or bronchial catarrh; consider further, how nowadays ontology is again attempting to creep into therapy in all sorts of disguises as we see it most markedly in the so-called specific methods of cure, and we shall not wonder that ontology has rapidly been able to gain such currency within so young a science as pathological microscopy as has even threatened its existence as a science. The cancer cells are regarded as pathognomonic for cancer, the pus cells as characteristic for pus.

With ontology the entire pathological teleology will disappear; cancer will no longer be a parasite of independent vitality maintaining its existence at the expense of another life, and against which the organism wages battle in order to destroy it. Suppuration will no longer be a curative measure of the organism, the pus bodies will no longer be gendarmes ordered by the state to escort this or that foreign intruder, who has come in without a passport, across the frontier; the fibrous tissue no longer will form the prison walls within which to confine such a foreigner.

In a well-known treatise written in 1849, "Die Einheitsbestrebungen in der wissenschaftlichen Medizin," Virchow further emphasizes his view that "the destruction of the ontological conception of disease is also a destruction of ontological therapy, of the school of the *specifics*. The subjects of therapy are not diseases but conditions; we are everywhere only concerned with changes in the conditions of life. Disease is nothing but life under altered conditions."

We see how the custom of regarding pathology as a kind of modified physiology dominated the whole German school. The great advance made by this school lies in the fact that it set as the goal of all medical science the attaining of an understanding of morbid processes, of the relations between the pathological phenomena.

"Das Kennen ist wichtig, aber das Begreifen is das Wichtigere und Höhere." With these words Wunderlich characterizes the aims of physiological medicine, and thus contrasts them with the purposes of the French school of medicine which confined its attention chiefly to the description of morbid phenomena, both the clinical phenomena and the pathologico-anatomical lesions. As we have seen, he and his colleagues opposed the efforts of the clinicians to establish clinical pictures of the various diseases, each disease following a characteristic course. On the other hand, such conceptions formed the foundation of the flourishing French and English clinical medicine of the time. This attitude of antagonism which was adopted by the Germans was not without consequences for the future of German internal medicine.

If we look at the whole evolution of German medicine in this fruitful period we find that it was primarily in the theoretical branches of medicine that the development took place. Experimental physiology received an enormous impulse and one physiological institute after another sprang up in the various universities. Under Virchow and his many disciples pathological anatomy developed into a powerful and quite independent science. As great an advance in general medical views as Bichat had produced by his general anatomy, was now affected by Virchow through his cellular pathology and through the thoroughgoing microscopical revision of the whole of pathological anatomy which now took place. It is entirely due to the circumstance that these great branches of science, physiology and pathological anatomy, now became emancipated from clinical medicine that it became possible to subject them to the thorough and accurate revision which was needed. Germany thus became a pioneer to other countries where such an emancipation was tardy in making its appearance or has to this day been only imperfectly accomplished.

What, now, was the position of clinical research during this powerful movement, what part was assigned to it, and how was it furthered?

In order to answer this question it will be natural to consider the activities of the two great clinicians who were the leading men at Berlin during this period, namely, Traube and Frerichs.

As already noted, Traube started on his scientific career as an experimentalist, and after he had obtained charge of a clinical department at the Charité Hospital in Berlin and was carrying on his work as a teacher of "clinical propaedeutics," he retained his interest in experimentation. He may be said to have founded experimental pathology in Germany and his best known clinical work was performed in intimate connection with experimental studies. For instance, in 1856 he developed his doctrine of variation in blood-pressure, and more especially of hypertonia as the cause of the cardiac hypertrophy which Bright had observed to be present in chronic nephritis. He based his conclusion chiefly upon experiments made by Ludwig and upon his own experiments on animals. In continuation of these investigations he described interstitial nephritis.

Perhaps, of still greater importance to clinical medicine were his investigations concerning clinical thermometry. In this he fulfilled another of the demands of physiology, that of exact measurement of the morbid phenomena. But it was not until Wunderlich by the advice of Traube had taken up this problem that the endeavor to introduce thermometry at the bedside became successful. To him, above all others, we owe it that the daily measurement of the temperature gradually became a necessary detail in the observation of patients. We are also chiefly indebted to Wunderlich for the demonstration of the typical temperature curves of the various diseases. It is interesting to see how through the recognition of these typical curves and their significance in diagnosis he was gradually led more and more to acknowledge that the various diseases ran typical courses, and he was, therefore, forced to adopt a point of view not dissimilar from that held by the French clinicians with their despised ontology. Indeed, we have just heard from his disciple, Strümpell, that Wunderlich, on his rounds, often looked more intently at the temperature charts than he did at the patients.

Traube's other clinical studies consisted chiefly in contributions to anatomical local diagnosis, especially of lung disease, and clinical medicine has, as we know, retained his name in the designation "Traube's space" for that part of the left pleura which lies below the lung. His system of diagnosis was based chiefly on pathological anatomy and especially on Virchow's teaching.

Frerichs, who became the leader of clinical medicine at the Charité in 1859, began his scientific career as a chemist and physiologist under Liebig. Nevertheless, in his first important clinical work, that on Bright's disease, published in 1851, he laid stress on the importance of independent clinical observations, and sought, on the whole, more than Traube, to emphasize their value. In this work on nephritis he

FRIEDRICH THEODOR VON FRERICHS
[1819-1885]

was the first accurately to describe uremia, and he attempted to discover its pathogenesis by means of experiments on animals, for he, too, recognized the great value of experimentation, though he looked upon it largely as an aid to clinical medicine. He desired that the latter should be founded on thorough chemical and anatomical knowledge, together with bedside observation.

This attitude of mind is revealed in his great work on the diseases of the liver, in which he described acute yellow atrophy. He made other contributions to medicine, mainly of a physiologico-chemical nature, such as his studies on leucin and tyrosin. Despite his marked chemico-physiological tendencies and interests, he, too, largely subordinated his clinical studies to pathological anatomy. It was above all Virchow's pathology which dominated clinical medicine everywhere at this time, and this was but a continuation of Rokitansky's pathological anatomy and just as dogmatic as the latter in regard to clinical problems.

Frerichs to a certain degree saw the mistake of letting anatomy predominate, but made only faint resistance, although he was annoyed by the purely personal antagonism between himself on the one side and Virchow and Traube on the other. This divergence was so great that Traube's and Frerichs' numerous and eminent disciples formed two separate camps which were far removed from each other, though they were equally scientific in their tendencies.

The strength of the new German internal medicine lay in its close connection with physiology and the new pathological anatomy. Before the English and the French, the Germans knew how to turn to account the immense advances which were being made in anatomy and histology, in physiology and physiological chemistry. Every clinician made it a point of honor to establish a laboratory in conjunction with his clinic, and from these laboratories issued a series of valuable investigations, but their themes were chemical, pathologico-anatomical and experimentally pathologic. Clinical observation, properly speaking, fared but badly. Nosology was required to fit into the framework supplied by Virchow's teaching and in certain main points this school stood for a decided retrogression in clinical medicine.

This was primarily the case with the study of tuberculosis. Virchow's investigation on tuberculosis, the chief innovation of which was his demonstration of the microscopical structure of the tubercle, led him to draw a sharp distinction between tubercles proper and what he called the caseous metamorphosis. All the processes, which Laënnec, drawing on his clinical observations, had combined into one single morbid unity, tuberculosis, were now divided into two main groups, all the tubercular phenomena being regarded as simple inflammatory processes followed by caseous metamorphosis. Likewise a definite distinction was again made between scrofula and tuberculosis, and tuberculosis occurring in the various organs was not regarded as the result of a general disease, but as local changes with a common tendency to caseation. This dualistic conception of tuberculosis was soon adopted by the German clinicians.

After Virchow had explicitly expounded this doctrine in his lectures on tumors (1862–65), Niemeyer became the special spokesman of the clinicians in a course of clinical lectures "Über Lungenschwindsucht" delivered at Tübingen in 1866. In sharp antagonism to Laënnec's view of tuberculosis as a primary, specific disease, he drew a distinction between the chronic, caseous and destructive phthisis, and the early, frankly tubercular condition. "Everything, which since Laënnec has been designated as infiltrating tuberculosis of the lung, is the product of chronic, especially catarrhal, pneumonia." Phthisis may begin as a croupous pneumonia, more frequently a chronic catarrhal pneumonia. Caseous necrosis, cavern formation, and new formation of connective tissue, the ordinary picture of chronic phthisis, may then develop. Tubercles may then supervene as a secondary complication in the advanced stages of phthisis. Famed is Niemeyer's sentence on this subject: "The greatest evil which can happen to a consumptive is that he should become tuberculous." In regard to intestinal tuberculosis a similar process was thought to occur. *Darmschwindsucht* was regarded as a tubercular eruption on the serosa, often occurring as a secondary complication of ulcerous processes in the intestine.

Turning the things topsy-turvy in this way, of course, produced great confusion in this important chapter of internal medicine and led to the habit of conceiving that the initial stages of phthisis in all instances were nonspecific apex pneumonias, catarrhal pneumonias, apex catarrhs or various forms of bronchitis and peribronchitis. The clinician was burdened with all these concepts when facing a case of incipient phthisis, and the general picture of tuberculosis which had been so clearly drawn up by Laënnec was thus again lost sight of. Moreover, these German clinical doctrines were not appreciably shaken by the fact that in 1865, Villemin demonstrated the inoculability of tuberculosis by experiment, and this inoculability was demonstrated for the infiltrating caseous form, as well as for miliary tubercles. At this time the connection between medical science in France and Germany was already beginning to be obstructed by the increasing political tension.

In its fear of, or aversion to, specificity and everything savouring of ontology, German medicine strayed back into confusion in other domains than that of tuberculosis. For instance, as regards diphtheria, Virchow maintained the conception of dualism, rejecting the French teaching which regarded diphtheria and croup as mutually interdependent, forming one specific disease. The confusion on this point really dates back to Rokitansky, who in his "Pathological Anatomy" (1844) invested the purely clinical concept of croup with an anatomical meaning, and included under the term "croupous inflammations" all diseases of the mucous membrane in which membranes were formed, whether the site of the lesion was in the throat, the larynx, the bronchi, uterus, the stomach or the intestine. Among these diseases he included pneumonia which he called croupous pneumonia on account of the fibrinous exudate in the alveoli. Somewhat later (1847) Virchow distinguished between croupous and pseudomembranous inflammation, and in consequence drew a sharp line of distinction between croup and pharyngeal diphtheria. As a result of these purely anatomical and extreme views, Bretonneau's doctrine of diphtheria gained no entrance into Germany. All doctrines of specific diseases were, as we have seen, denounced, and it did not enter the minds of German clinicians that there could be any connection between croup and pharyngeal diphtheria.

In an exactly similar manner Hebra identified variola with varicella in his exposition of the diseases of the skin in Virchow's "Handbuch der speziellen Pathologie und Therapie," though as early as 1766 varicella had been described by Heberden as a specific disease. Anatomically, the two conditions

RUDOLF VIRCHOW
[1821-1902]

were alike, and they must therefore after Hebra be regarded as varieties of one and the same disease, and as a necessary corollary a case of varicella might give rise to real smallpox.

These great and confusing errors of German medicine were only rendered possible through a failure to comprehend and respect the clinical, nosographical method. This attitude of mind, which characterizes Virchow and his pupils, was in part an inheritance from the new school of Vienna. Virchow maintained that the function of clinical medicine was to raise questions, pathological physiology to answer them, and the whole school followed his lead.

But not only pathological anatomy, but also physiology and experimental pathology took their share in discouraging clinical medicine, which during this period lost that veneration for its own problems which is so necessary, and it then became in a great measure reduced to a kind of accessory science subordinate to pathology and physiology.

It is interesting to read the judgment pronounced on clinical medicine by one of the most prominent of German clinicians, Naunyn, in a retrospective survey written in 1908, "Die Berliner Schule vor 50 Jahre." He was himself one of Frerichs' disciples and is universally known for his epoch-making studies on diabetes through which his name and that of his school have become inseparably associated with our knowledge concerning acidosis and pancreatic diabetes.

He writes as follows:

> Not until very recently did German internal medicine take a share in the development of nosography, semiology and diagnostics, and that this occurred so late was due to the physiological school.
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> It was the physiologist, Joh. Müller, who ended the domination of "Naturphilosophie" in his textbook on physiology published in the thirties. In internal medicine, especially, the influence of this philosophy was still very great and just here Müller's work as a deliverer was especially felt. For this reason modern clinical medicine has flattered itself with the name "physiological." But it happened that the enthusiastic advocates of the new movement, in their exaggerated zeal sought to find in physiology not only the direction of their activities, but also the decisive last word in pathological and specially in clinical questions. The clinical pictures were only "recognized" in so far as they reflected physiological laws; it was then attempted to read the separate

symptoms in the light of these often very distorted physiological images. Often one constructed them oneself instead of finding them by faithful and impartial observation. Of Traube it must be said that he, too, often made clinical medicine the servant of physiology, losing himself in petty details and subtleties in symptomatology in order to preserve the most intimate connection possible with physiology, and other clinicians did the same.

All the prominent representatives of this generation of clinicians realized, no doubt, that a scientific nosography and symptomatology can only be based on clinical observation. They all made valuable casuistic contributions; for instance, Traube (to mention only caseous pneumonia and the coal-dust lung), Frerichs (acute atrophy of the liver, pulmonal stenosis, cerebrospinal sclerosis), Friedreich (atrophy of the muscles, Friedreich's disease), Griesinger (pseudohypertrophy of the muscles). Yet how far behind the French and English were we Germans in our estimate of casuistry? We need only think of Duchenne de Boulogne.

The criticism here directed by Naunyn against the clinicians who were too much influenced by physiology, reminds us of Sydenham's and Locke's censure of the representatives of chemiatry in the seventeenth century, and indeed, the fault in both groups arose from the same cause, namely, an overweening pride in speculation and laboratory wisdom as contrasted with an interest in living nature as she appears in the motley world of morbid phenomena.

It is, as we see, only a scanty harvest of nosographical advance which Naunyn can present to us from this exuberant period of German medicine, and this paucity speaks for itself.

But the next generation of German clinicians took up clinical nosographical problems in earnest. Virchow's influence had been weakened, Traube had died and been replaced by Leyden and he together with the aging Frerichs and a number of prominent clinicians throughout Germany inaugurated a new and more clinical era in medicine, while Berlin was growing to be the capital of the new German empire. On this subject Naunyn writes:

> Not until after 1870 did we come into the full enjoyment of building up our complexes of symptoms, our clinical pictures empirically. The more earnestly we became absorbed in our cases the more did our interest in casuistry increase, and now our good training in the methods used in anatomy, physiology and chemistry (the technique of examination) made

good. The demand for a thorough examination of the cases gained more and more ground as the condition for "a serviceable case." These endeavors soon bore ample fruit; thus in neurology, the abdominal diseases, the diseases of the blood, but above all and most brilliantly in the pathology of metabolism. In the works on metabolism in fever and diabetes German clinical medicine early asserted its superiority. We owe this to our physiological school, the Pettenkofer-Voit school at Munich. It was a very long time before the value of such investigations began to dawn on the mind of the French.

So we see how German physiological medicine was in the main preparatory, leading up to the new clinical era. It contributed to clinical medicine chiefly through the stimulus it gave to the introduction of new methods of investigation, graphic, microscopic and chemical. These methods were developed chiefly by the physiologists and chemists, but the clinicians quickly adopted them. We may mention, for instance, the introduction, in 1852, of methods for the counting of hemacytes by the physiologist, Vierordt, and his employment, in 1855, of the sphygmograph for investigating the pulse, the measurement of the color of the blood by the anatomist, Welcher, and the invention of methods for the examination of the urine by the physiological chemists, Trommer and Heller. In this connection we may also mention the invention of the ophthalmoscope in 1850 by the physiologist, Helmholtz. This initiated a flourishing period in ophthalmology in Germany and was quickly followed by the introduction of Garcia's and Türck's laryngoscopes (1854 and 1857) and of Troeltsch's otoscope (1856).

In the endeavor to introduce physiological methods into the clinic contemporary French scientists bore an important part. Thus we find Andral, one of the older members of the Paris school, advocating clinical thermometry in 1841, and about the same time he began to determine the content of fibrin and corpuscles in the blood, and of albumin in serum, by weight, and he introduced this as a clinical method. By his studies on the blood, of which he has given a summary in his "Essai d'hématologie," which appeared in 1843, Andral made a weighty contribution to what may be called the physiological clinic. Just as his "Clinique Médicale" has stood as a model for anatomico-clinical studies, so his "Hematology," by its methodical lucidity, has served the same purpose for all later physiological clinical investigations. He began his studies on the blood by making a quantitative investigation of the components of the blood in healthy individuals and in various animals, and then he investigated the condition of the blood in a series of patients suffering from various diseases. By these studies he laid the foundation of future hematology.

The Paris physiologist, Marey, greatly advanced clinical medicine in another way, namely, by the development of various graphic methods. Not until this had been done could serviceable sphygmographs, cardiographs, etc., be constructed.

During this period the same conflict of ideas that was taking place in Germany was occurring in France. Claude Bernard, the successor of Magendie, was not only brilliantly continuing the work in experimental physiology, but at the same time he was making strenuous endeavors to introduce experimental methods into pathology. In this attempt he himself made important contributions to medicine, such as those resulting from his well-known investigations on glycosuria.

To him experimental medicine was synonymous with scientific medicine. He set forth his views on this matter, especially in his "Introduction à l'étude de la médecine expérimentale," which was published in 1865. Here he set down clearly and convincingly the part played by experimentation in medicine and described its special methods, one might say, its philosophy. Less clearly did he see the importance of clinical observation as a scientific method. His views on this subject are perhaps most clearly seen in a passage from his "Leçons sur le diabète," which appeared in 1877. He says: "La médecine, riche des faits acquis à l'hôpital, peut maintenant le quitter pour aller dans le laboratoire. En prenant la forme de médecine expérimentale, elle devient science pure."

In this invitation to desert the bedside in favor of the laboratory he expressed the real tendency of the old physiological medicine. He looked upon the work of clinical medicine at the bedside as essentially concluded. He seemed to have no eye for the fact that the problems disclosed by the examination of patients were, as yet, far from solved. To him diseases represented well-known phenomena mature for laboratory study.

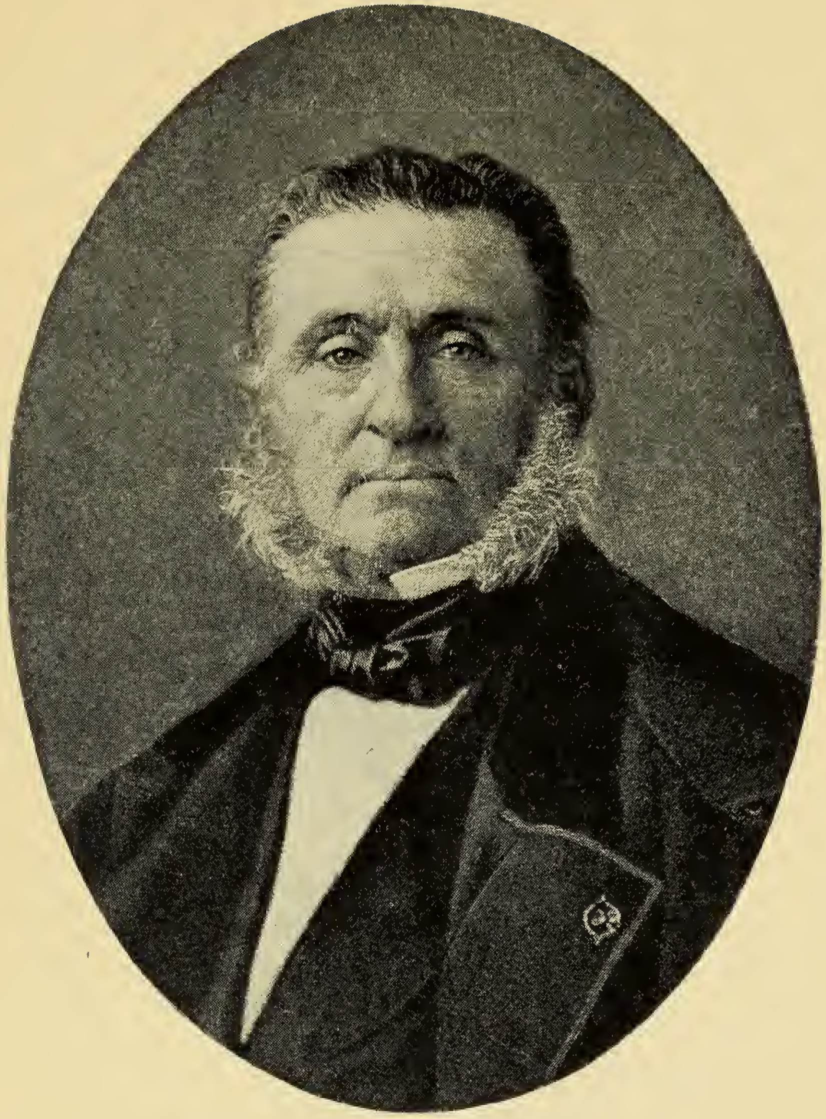
He had not the slightest comprehension of the continual growth, the continual scientific development and transformation of conceptions of diseases which take place in clinical medicine. A similar point of view is still sometimes taken by physiologists and experimental pathologists who have received their training far from the bedside. For instance, Pawlow develops quite similar views in a lecture delivered in 1900 entitled "Das Experiment." He writes here about clinical medicine that "in the thousand years of its existence it has succeeded in definitely establishing the types of the different diseases and in giving a nearly perfect morphology of the pathological conditions." Therefore at present, experiment is the only fruitful method in medical research.

Undaunted by such want of respect for clinical scientific work by the physiologists, French clinical medicine of this period maintained the tradition of the Paris school and continued its nosographical work, but the conflict between the divergent views often resulted in controversy. The chief leaders of clinical medicine in France at this time were Lasègue and Trousseau.

Lasègue is chiefly known as an eminent neurologist. To him we are indebted for the first description of the mania of persecution, of nervous anorexia and many other excellent observations. But as editor of the *Archives Générales de Médecine* he was also an active medical journalist and was much concerned with the problems arising from a comparison of the methods employed by the German physiological school with the more clinical methods employed chiefly by the French and English, especially the problem concerning the relative value of these two types of work for the advancement of medicine.

Although Lasègue apparently failed to understand the great progress which was gradually being made by the employment of the more exact methods of investigation and experimentation, he clearly saw the harm resulting from the subordination of clinical observation to the reasoning of chemists and theorists. He states:

> But fortunately, the danger resulting from the opinion of these physiologists that they can disregard medical observation is less than one would think. They observe little, and they observe badly. They explain much, or rather, they explain everything, and they pass quickly from hypothesis to practice. But after the most adventurous excursions they all end peacefully



ARMAND TROUSSEAU
[1801-1867]

at the same point, the point which had already been reached, and medicine proceeds undisturbed, though with caution, on its onward march.

In Trousseau France had a clinical observer of the very first rank. His description of diphtheria in its various forms and stages is well known. He advocated the introduction of tracheotomy and thoracocentesis, and his studies on typhoid fever, scarlatina and many other diseases are of great value. In his famous "Clinique médicale de l'Hôtel Dieu" (1861) he repeatedly emphasized the great importance of observation at the bedside: "To know the natural course of the diseases is more than one half of medicine." While joining issue with the theorists and especially opposing the propensity of the chemists to intrude into the domains of clinical medicine, he lucidly defends the clinical, nosographical method, which the Germans had rejected. He was the disciple and warm admirer of Bretonneau and supported his doctrine of specific diseases. Indeed it was in the eloquent lectures of Trousseau that this doctrine assumed its ultimate form.

Concerning the specific nature of disease he says:

This important question dominates all pathology, all therapy, in a word, all medical science. The natural history of the diseases resembles that of the animals and plants; it deals, in the same way, with specific properties which separate the species.

In his clinical lectures he adduces a series of examples of specific properties of diseases. Particularly striking is the specific character of syphilis. After coitus impurus a small vesicle on the penis is often observed. In one case this is a simple herpes praeputii, the vesicles of which dry up and disappear without leaving any consequences. In another case it is the beginning of an ulcus induratum with succeeding general manifestations of disease. At the onset both lesions have the same character, but in the second case, additional specific properties of the greatest importance are present, and he clearly formulated the view which was also Bretonneau's: "That which gives the specific diseases their immutable properties is not the quantity but the quality of the morbific cause." To each particular cause of disease the system replies with specific and characteristic phenomena. For instance, in chronic lead-poisoning the morbid phenomena are extremely characteristic and are obviously distinct from the phenomena which are associated with chronic mercury poisoning.

Trousseau has here made use of an argument which is in reality conclusive regarding the whole question of the right of nosography to be called a scientific method. That which justifies the effort to shape definite clinical pictures, to group cases which show a characteristic symptom-complex, and exhibit a typical course—and to describe the result of our labor as a disease-entity—is after all the conviction that every time we can thus set up a separate disease, we are at the same time on the track of a specific morbific cause. Hence the work of the nosographical method by no means consists in a mere description of the phenomena but also represents an endeavor to understand their interconnection.

What obstructed the advance of clinical nosographical research at this period was, primarily, the complete lack of knowledge concerning the most frequent, specific etiological factor in pathology, namely, infection; but no long time was to pass after Trousseau made the afore-cited remarks before the utter darkness would give way to light.

Indeed, Pasteur had already performed his brilliant experiments relating to fermentation and putrefaction, and Trousseau saw as clearly as Lister and Davaine the significance which these researches might have for disease, and he saw also that the doctrine of the discovery of specific fermentations gave great support to the whole doctrine of specific diseases.

When Trousseau died in 1867 Pasteur was in the midst of his fight against the silkworm disease, and he had thus started upon the series of discoveries in the field of pathology which followed each other in rapid succession during the following decades and which revolutionized theoretical as well as applied medicine and surgery.

PART IV

THE BACTERIOLOGICAL CLINIC

By Pasteur's fundamental experimental work, the fact was established that a whole series of diseases is produced by certain distinct microorganisms, and thus the nature of specificity was at least in part unveiled. Sydenham, Bretonneau and Trousseau had been right; there were really specific diseases and specific morbific causes. Some of the most disputed problems of clinical medicine of the last centuries had suddenly been elucidated. The ever-recurring craving of the clinicians for "ontology," for fixed categories of diseases, was, then, fully justified. The *quid divinum* of the diseases referred to by Sydenham and Bretonneau had now taken definite shape, and a reconsideration of the concepts of disease from an etiological standpoint was now to be undertaken, since at last the nature of the cause of the commonest and the most formidable diseases had been revealed.

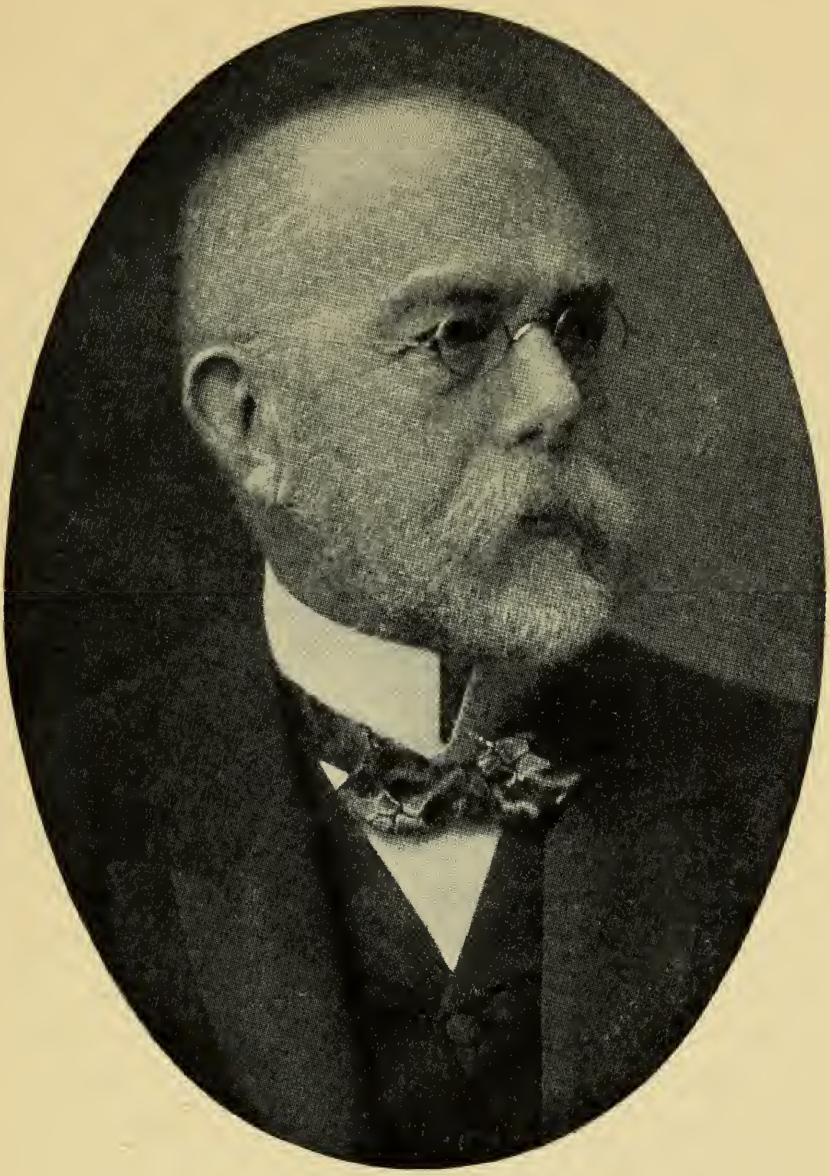
The result was bound to be a complete revolution of ideas and aims, more especially in Germany, the home of the physiological school. Hence, while the new medicine founded on Pasteur's and Koch's work met with an enthusiastic sympathy from the whole of the younger generation, it received a somewhat sullen and cool reception among the older group of physicians, among whom Virchow had been and still was the leader. Actual opposition was, of course, out of the question, but the leap from Virchow's to Koch's medicine was too great to be made painlessly, and as science marched onward, things grew no better. In proportion as ample amends were made to Sydenham and his successors, Virchow's prestige diminished. As Behring wrote in 1912: "Sydenham was everything that Virchow had energetically fought; he was an ontologist, specificist, humoral pathologist and etiological humoral therapeutist." Of course, Virchow's fundamental work in microscopical and pathological anatomy did not lose in value, but new views concerning the pathology of all infectious diseases now prevailed, and this had a revolutionizing effect on clinical medicine.

Moreover, a new technique in the examination of patients, which could, without difficulty, be applied at the bedside, was now being established. Following the discovery of methods for staining bacteria, developed by Ehrlich and Weigert, and later by Gram, Ziehl and others, the demonstration of the specific bacterium concerned in a given case could often be made at once, and so a specific diagnosis be immediately established. This was of great value in clarifying and developing the clinical pictures of specific diseases, for now the non-specific cases could at once be set aside and only the cases in which the bacteriological examination gave positive results be retained for comparison.

Specific staining reactions were found for the tubercle bacillus, the leprosy bacillus, and the gonococcus, and even without such specific methods, it was possible to distinguish, at least with a considerable degree of certainty, such bacteria as the pneumococcus, the meningococcus, the streptococcus, and others. In addition to this, special cultural methods were devised which permitted the ready detection of other bacteria, as the diphtheria bacillus, the typhus bacillus, the cholera spirillum, etc. This made possible early specific diagnoses in a large group of diseases. Yet another way to specific diagnoses was later opened to clinical medicine by the discovery of the various specific serum reactions, such as the agglutination phenomenon, which was applied in the diagnosis of typhoid fever by Widal, and the fixation of complement reaction, which was applied by Bordet and Wassermann to the diagnosis of syphilis.

As a result of the employment of these specific diagnostic methods there occurred a revision of all existing clinical categories of infectious diseases, including most of the acute inflammations localized in the various organs. Diseases now came to be viewed from an etiological point of view, and the efforts of clinicians were directed towards replacing as far as possible the nosography founded on anatomy by a nosography founded on the morbific causes.

This was not a difficult task so far as the typical acute infectious diseases were concerned. As we have seen, the picture of these diseases had been usually constructed with regard to their general clinical symptoms, characteristic course and epidemiology; they were quite obviously etiological entities, only waiting to have their causes demonstrated. With respect to the more atypical diseases, such as the suppurative



ROBERT KOCH
[1843-1910]

inflammations in the various organs, greater and more astonishing alterations in prevailing concepts were now rendered necessary. For instance, in 1880, Pasteur announced that he had found the same bacterium as the cause of the furuncle and of acute osteomyelitis. As Charrin has stated, this communication was greeted with silence by the more polite, so absurd did it seem, but it was only the prelude to a series of discoveries of a similar kind.

The changes in clinical concepts brought about by the discoveries of this period were probably greatest in the case of tuberculosis. By Koch's classical work on tuberculosis, which appeared in 1881, the unity of this disease as regards etiology was established. Laënnec's views, dating from the beginning of the century, now received their ultimate proof. Villemin's experimental work from 1865 had received its corroboration, and Virchow's dualistic doctrine had been found to be an error. Tubercle bacilli were demonstrated by Koch not only in the various tuberculous tissues of the lungs, but also in the tissues of other infected organs, in tuberculosis of the intestines, of the bones, tumor albus, lupus, glandular tuberculosis and in animal tuberculosis. The staining technique for tubercle bacilli was soon developed by Ehrlich's introduction of aniline staining and acid decolorization and by Ziehl's substitution of carbolic solution for aniline oil, so that a bedside examination could quickly be made. Thousands and thousands of examinations were now made, at first in Germany, but very soon in hospitals all over the world, and the clinical aspect of tuberculosis, which was once so complicated, was soon enormously simplified.

All the different types of chronic pneumonia, apex catarrh, apex pneumonia, etc., which had been set up by Niemeyer and his successors, as well as Buhl's desquamative pneumonia and other similar affections of the lungs, disappeared, and the picture of tuberculosis of the lungs as it had been drawn up by Laënnec sixty-five years before, came more and more clearly into view. Similarly, the various forms of caries and tuberculous affections of the joints, as well as the glandular affections and other scrofulous complaints, were now seen with new eyes. The tuberculous forms were recognized as such and were then without difficulty clinically distinguished from other kinds of affections of the bones, joints, or glands.

In brief, all the various tuberculous affections of man were now united into one single picture of a specific, chronic, infectious disease with a uniform etiology.

Something similar took place in the case of diphtheria. After Loeffler had discovered the bacillus of diphtheria in 1885 and a clinical, diagnostic method, involving the cultivation of the bacteria from the membrane, had been devised, it was very soon proved beyond contradiction that croup and pharyngeal diphtheria were due to one and the same infectious agent and were manifestations of the same specific disease. As in the case of tuberculosis, the dualistic conception had to give place to the older and clearer conception of a unity, which we owe, in this case, to Bretonneau's clinical acumen.

Even in the case of certain other infectious diseases in which no pathogenic microbes could be demonstrated, the evidence that each was etiologically distinct became more and more convincing, and this, of course, influenced the clinician's whole attitude toward the clinical phenomena. In this connection it is interesting to trace the changes which occurred during this period in the attitude of physicians toward the other great chronic infectious disease, syphilis. The changes were undoubtedly directly related to the development of the etiological point of view in clinical medicine, though the specific microbe of syphilis was not discovered until 1905 by the German zoologist, Schaudinn. During the latter half of the nineteenth century the clinicians gradually grouped, and even identified, with this disease a series of organic affections of the nervous system, heart and aorta, which had previously been clinically and anatomically well observed and studied, but which hitherto had not been thought to have any connection with syphilis.

This movement in clinical medicine concerning syphilis illustrates especially well certain aspects of the methods of nosography. In clinical medicine it has been the aim to endeavor further to classify, on an anatomical basis, all those affections in which the same symptoms occur, that is, to classify them according to the seat of the diseases and to the different lesions of the organs involved. For instance, cases showing paralysis are not all grouped together but are placed in various groups arranged according to the lesions of the organs involved in the disease. The same is true regarding cough or vomiting or any other symptom. The result has been to establish a series of clinico-pathological, instead of pure symptomatic, pictures. Side by side with this, however, there has been a sort of synthetic movement, an attempt to combine in one collective picture certain groups of affections in which, though different organs are involved, yet there is exhibited a certain uniformity in finer structural changes. We saw how this took place in the case of tuberculosis, and the same has gradually occurred in the case of syphilis. An important and very valuable piece of work which was largely instrumental in bringing about this synthetic movement in the conception of syphilis was the description by Virchow of the anatomical alterations in the various organs in a group of affections considered syphilitic. At that time, however, large groups of affections now known to be syphilitic were not thought to have any direct relation to this disease.

This was true of one of the most characteristic nervous affections, namely, tabes dorsalis. This condition was first accurately described by the French clinician, Duchenne de Boulogne, as a distinct and well characterized clinical complex of symptoms, whose chief phenomenon, locomotor ataxia, he had described in 1856. Although the underlying anatomical lesion of the posterior columns of the spinal cord had previously been seen by Cruveilhier, and Romberg had described several of the symptoms, to Duchenne is due the credit for having first definitely outlined its clinical features. His study was further elaborated by Trousseau to whom it was at once obvious that this was a well delimited pathological condition. Nevertheless the attempt was made on physiological grounds to associate this condition with the ataxia associated with affections of the cerebellum and with other spinal lesions. Trousseau protested against this and maintained that "a disease showing such constancy in its symptoms and in its lesions must be conceived as a specific disease," which meant, according to Trousseau's way of thinking, that it was an etiological unity.

Time proved the correctness of his opinion. In 1876 Fournier advanced the hypothesis that syphilis was the cause of tabes, and the following decades saw the accumulation of an ever-increasing number of observations and statistics in favor of this hypothesis. Nevertheless, for a long time it was opposed and rejected.

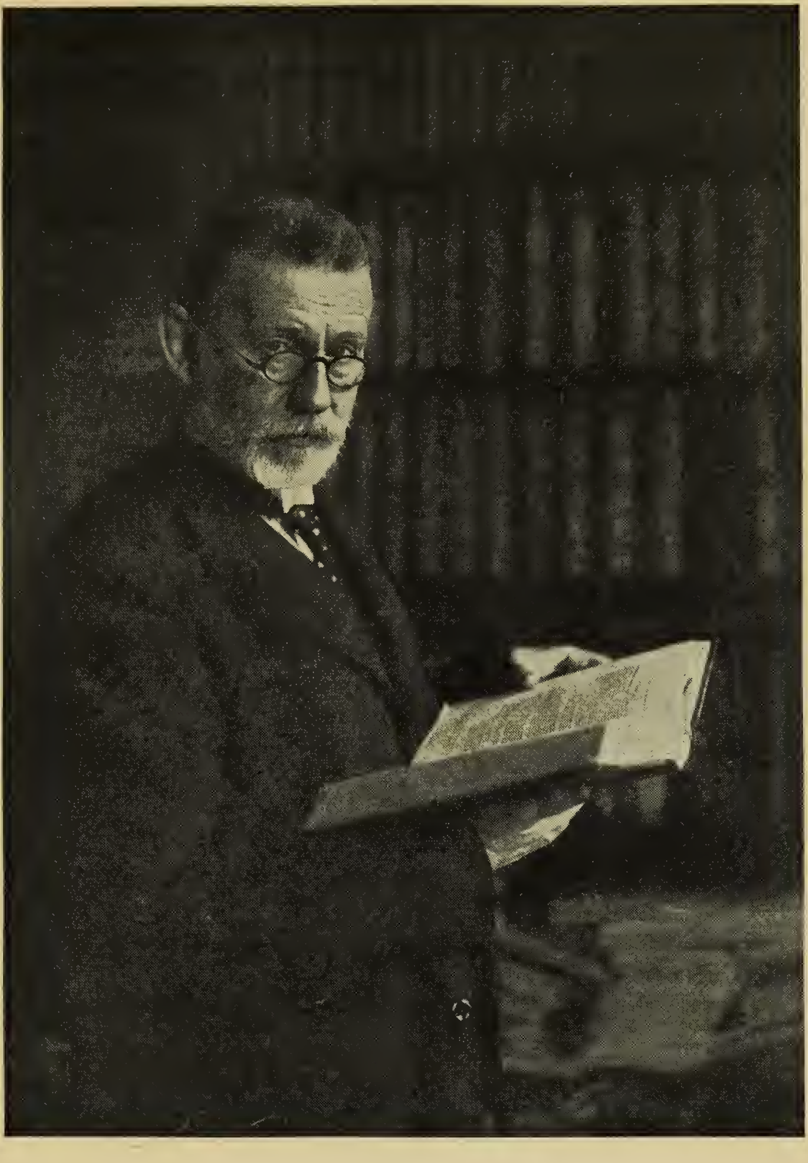
LOUIS PASTEUR
[1822-1895]

A similar discussion occurred in regard to general paralysis, the morbid picture of which was first drawn up in 1822 under the name of arachnoiditis chronica by Bayle. This condition was first conceived of as a syphilitic affection by the Germans, Esmarch and Jessen, in 1857. As in the case of tabes, the method of investigation of this question consisted in the collection of statistics relative to the frequency of occurrence of syphilis in the history of patients suffering from the disease. In 1873 Jespersen at St. Hans Hospital in Denmark produced statistics which established the truth of the contention of Esmarch and Jessen, but these statistics received little attention. Gradually confirmatory evidence accumulated, but, as in the case of tabes, the new view made but slow headway, and it became customary to class these two affections together as parasyphilitic, not as actually syphilitic affections. Indeed it is only very recently that all opposition to the idea that general paralysis is a true syphilitic manifestation disappeared. In the first place, the introduction of spinal puncture made possible the study of the changes in the spinal fluid. Then the discovery of the method of complement fixation permitted an accurate diagnosis of syphilis to be made. Next in 1905, Schaudinn discovered the etiological agent of syphilis, the Spirochaeta pallida. Finally, Noguchi demonstrated the presence of this organism in the brain of persons suffering from general paralysis. Only then did all opposition disappear and general paralysis and tabes come to be universally recognized as due to syphilitic infection and the two symptom-complexes regarded as component parts of the complex clinical picture of syphilis.

A similar course of events transpired in relation to certain affections of the blood-vessels, particularly, aortic aneurysm. Vesalius observed this affection at the post-mortem table, and in the sixteenth century Fernel and Ambroise Paré believed that it could be caused by syphilis. These old observations did not, however, have any influence on the current view. The symptoms and pathological anatomy of aneurysm had been well described in the first half of the nineteenth century. In 1876 the Englishman, Welch, asserted that syphilis was the most frequent cause of aneurysm, and in the following year, the Norwegian, Heiberg, expressed the same opinion. In the following decades the view that syphilis was the only or chief cause of aneurysm was little by little almost universally accepted. As in the case of the nervous affections, the chief evidence presented in support of this view consisted of statistics. Thus Rasch in Copenhagen demonstrated the presence of syphilis in 81 per cent of the cases of aneurysm and Heller at Kiel in 85 per cent of the cases. In addition to the statistical evidence, the occurrence of a characteristic syphilitic affection of the great vessels, with peculiar specific anatomical features, was demonstrated. Nevertheless, it still required the evidence obtained by testing patients by the reaction of complement fixation (Wassermann's reaction) to sweep away the doubts which still remained.

So we see how the characteristic picture, now so well known, of the syphilitic infection, not only of the skin and the mucous membranes, but also of the internal organs, has been laboriously put together in the course of the century, and to this day, no doubt, the last stage has not yet been reached in the delineation of visceral syphilis in its various aspects. But an etiological unity has now been created out of all the various syphilitic affections which would excite the admiration of the older ontologists. Moreover, this definitely specific disease has long had its own specific therapy which has reached its highest development in the introduction of Ehrlich's salvarsan.

For hand in hand with the study of the etiology and pathogenesis of the infectious diseases there has proceeded a therapeutic movement of signal importance. Here again it was Pasteur who made the beginning by his ingenious experiments concerning the prevention of rabies even after infection had occurred. His mode of attack of the problem consisted in first inducing a decrease of virulence in the virus, and then employing this virus for therapeutic vaccination. Thus the way was mapped out for the discovery of specific remedies for specific diseases. The effect of Pasteur's discovery was overwhelming and the mind was carried back, quite naturally, not only to Jenner, who who was the originator of the first protective vaccination, but also to Sydenham who first advanced the demand for specific remedies. This was indeed for a long time considered a great defect in Sydenham. As a matter of fact, there is hardly anything for which Sydenham has been so severely



PAUL EHRLICH
[1854-1915]

taxed by later physiological medicine as for his doctrine of specific remedies. Wunderlich, for instance, wrote in 1859 concerning Sydenham:

> He was a sober and comparatively unprejudiced observer, but he was no acute thinker. His vagueness of thought deluded him into ideas which led his successors to take the wrong paths. To such ideas belong his postulates concerning a distinct nomenclature and specification of the different forms of diseases, and his delusion that specific remedies may be found for all or most diseases.

On the other hand, Sydenham's hope had induced the nosologists, who followed him, to conduct an eager search for specific remedies for all the different diseases which they described and named. As Wunderlich has pointed out, this actually led to the grossest empiricism. "If a morbid species had been ascertained, a formula of cure was immediately in readiness on the authority of some professor. Thus everything possible was being done for the patient, and the scientific conscience of the physician was salved." The critical pathologico-anatomical school had completely put an end to this belief in specific remedies, but, on the other hand, there was substituted the gloomiest nihilism in therapy. In place of this the physiological school sought to develop, through physiological arguments and pharmacological experiments, a therapy which claimed to be scientific and rational in that it was attempted to modify the treatment to suit the individual. As a matter of fact the form of treatment recommended was merely palliative and symptomatic and in the main led to disappointment. In fevers the temperature was lowered but the disease developed in the usual way; pain was alleviated by morphia and other anodynes, but the course of the disease was not appreciably altered, and gradually clinicians had been compelled to center their hopes on the future and depend on the advance of science. Now suddenly the possibility of specific remedies again appeared; this time in a new and more attractive shape, not as a healing herb accidentally discovered, but as a specifically reacting substance logically derived through a series of scientific experiments.

This possibility, as we know, developed into fact. In continuation of Pasteur's work, Roux and Behring introduced serum therapy, and as a further result of experimental pathology Ehrlich created chemotherapy.

By these great discoveries and inventions specific pathology had been firmly enthroned and specific therapy had become the hope of physicians. This faith was not seriously diminished even by Koch's premature attempt to introduce a specific therapy for tuberculosis in his well-known tuberculin cure. As yet such a specific therapy in this disease has not been found, but who doubts but that we shall obtain it in some shape or other at some future time?

As we have seen, etiological researches on infectious diseases created a firm basis for the nosography of these conditions and brought clarity into the conception concerning their pathology. But this applies only to the infectious diseases, and all other diseases were left unaffected by this movement.

PART V

FUNCTIONAL DIAGNOSIS

As soon as German clinical medicine emancipated itself from the Virchow-Traube tradition with its overemphasis on animal experimentation as the principal method of scientific research, it turned actively, as we have seen, to general nosographical work, a method of study that had always attracted many gifted scientists in England and France. This change in direction was most plainly evidenced when the new *Zeitschrift für klinische Medicin* was established by Frerichs and Leyden in 1880. In the introduction to the first volume Frerichs asserted the independence of clinical medicine and opposed the tendency for the theoretical branches of science to predominate as detrimental to progress in medicine. The main method in the study of disease, he maintained, must be the collection of information at the bedside by every means available to modern science. Experiments on animals are indispensable when observation of patients alone does not provide means for solving the problems which are involved, but "experimental pathology should not, as sometimes happens, lay claim as an independent science, to the leading rôle in studying diseases. This method is as little suited to this end as was once chemistry, or physics, or morphology. The decisive method of approach is and always will be the observation of patients."

These views stimulated German clinicians to strenuous activity, and as Naunyn has pointed out, the sound physiological training of these men helped them to obtain important results. In the first volumes of the above-mentioned periodical Basch published his important measurements of the blood-pressure in various morbid conditions. Ehrlich began the publication of his studies on leucocytes in diseases of the blood, and Leyden continued his studies on diseases of the nervous system. German medicine can boast a number of famous clinicians who, at this time, worked in a similar manner, such as Naunyn, Erb, Westphal, Nothnagel, Quincke, Kussmaul, and Friedreich, while at the same time Duchenne, Vulpian, Brown-Séquard, Charcot, and Marie in France, Gull, Hughlings-Jackson, Gowers in England, and Osler, Beard, Huntington, Hammond and Milroy in America, all made weighty and primarily nosographical contributions to internal medicine. Among Scandinavian scientists of this school we may mention chiefly the Danish neurologist, C. Lange, who in 1872 described chronic spinal meningitis as the cause of tabes dorsalis and Magnus Huss of Sweden who about the middle of the century described the clinical features of chronic alcoholism.

All these discoveries of new morbid pictures and new diseases and the elaboration and extension of knowledge concerning those already familiar depended primarily upon the thorough observation of patients and the examination, by accurate methods, of the morbid phenomena which they exhibited during life, and the demonstration post mortem of the underlying lesions, *la méthode nosologique ou nosographique*, as Charcot called this method which he, himself, employed so successfully in neurology. It was by this method that he succeeded in establishing such clinical entities as amyotrophic lateral sclerosis and disseminated sclerosis, and further, that he developed the application of Trousseau's doctrine of *les formes frustes*, *i.e.*, the less

JEAN MARTIN CHARCOT
[1825-1893]

typical, or as it were, half suppressed examples of disease which in every malady group themselves round the outspoken and characteristic forms. In a lecture delivered in 1882 Charcot described the principles of research which he followed and discussed, more especially the nosographical method. In order to emphasize the range of the method he referred to Duchenne de Boulogne's incomparable work in which he established those great types of disease known as progressive muscular atrophy, infantile paralysis, pseudohypertrophic paralysis, glossolaryngeal paralysis and locomotor ataxia.

Cette création a peuplé d'êtres animes, vivants, conformes à la réalité concrète, reconnus de tous, des cadres jusque-là restés vides ou remplis de formes confuses, cette création appartient toute entière à la méthode nosographique.

Next he described how the method, without change of character, had been extended by including the study of pathological anatomy and how it had thus obtained still further support. Finally he showed how the doctrine of localization, applied to the pathology of the nervous system, had given to nosology a physiological as well as an anatomical basis.

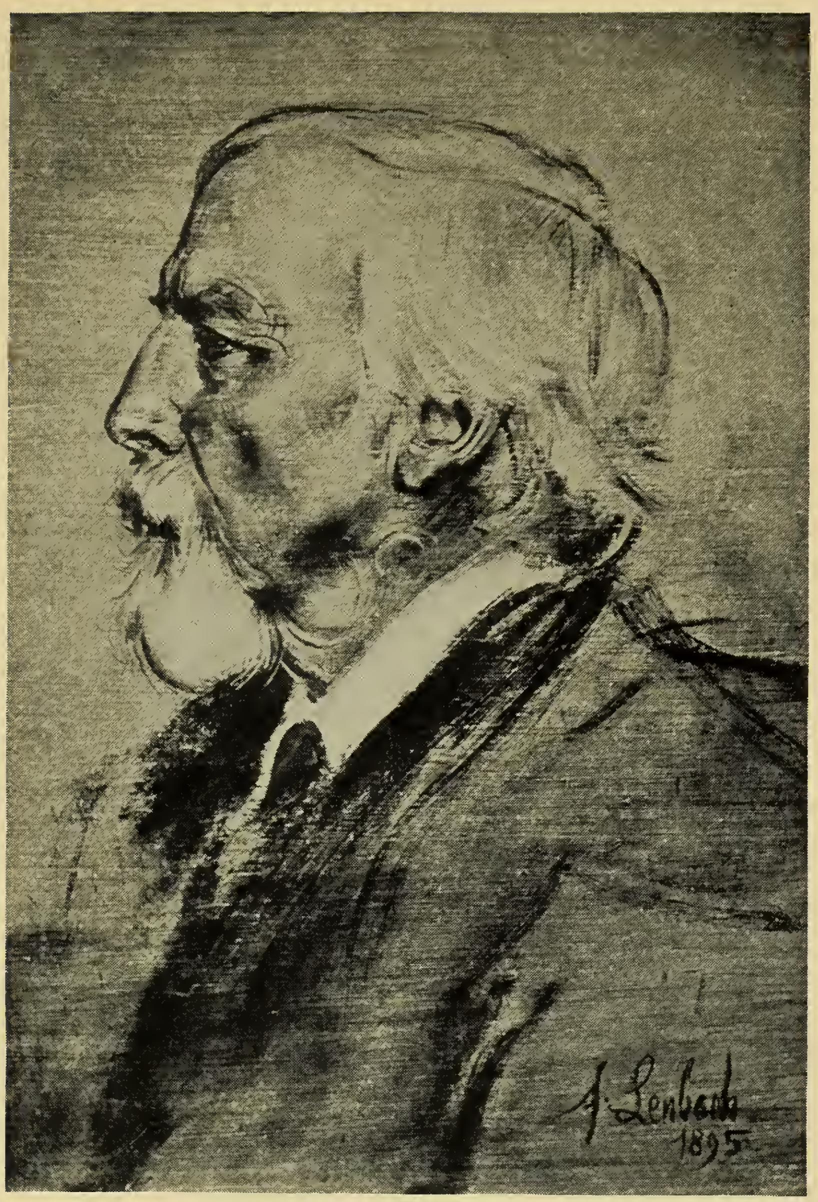
It was plain to him that the fundamental sciences were the source from which clinical observation and analysis must always derive their impulses for advance. "Sans rénovation scientifique, elle deviendrait bientôt une routine attardée et comme stéréotypée," but he concludes by emphasizing the supremacy of clinical observation: "Le rôle préponderant, la jurisdiction suprême devra toujours appartenir à l'observation clinique."

During this period neuropathology reached its highest level since the nosographical method is particularly well adapted to be applied to this branch of pathology.

Meanwhile a new scientific movement had been initiated in Germany which was soon to become of great importance in the development of clinical medicine. This movement was inaugurated by Kussmaul, one of the most prominent clinicians of Germany. At Freiburg, in 1867, he began to employ the hitherto little noticed and less used stomach-pump in the treatment of dilatation of the stomach associated with stagnation of its contents. The results he obtained were astonishingly favorable and created the greatest sensation in the medical world. Kussmaul saw at once that in emptying the stomach by means of the stomach-pump a method had been gained which was not only of the greatest therapeutic interest, but one which might also acquire significance from a diagnostic point of view and also be of value in the further study of gastric disease. This opinion was very soon corroborated. Only a few years later (1871) Leube proposed that the action of the stomach should be examined by giving patients various foods and then, after a certain time had elapsed, withdrawing and studying the contents of the stomach. One could then learn how quickly the stomach emptied itself of food, and how far the food had been digested at any given time. By digestion experiments with the gastric contents, made with or without the addition of hydrochloric acid, he was able to demonstrate (1873) that there is sometimes a deficiency of acid in the stomach.

In 1875, at the suggestion of Jürgensen and Ewald, the impractical stomach-pump was replaced by soft tubes, and this made the method much more convenient. In the following years this new physiological mode of investigation was eagerly and widely applied. Research took place, especially at Kussmaul's clinic at Strasburg where Szabo demonstrated the difference between free and combined hydrochloric acid (1877) and v. d. Velden showed (1879) that free hydrochloric acid was wanting under certain conditions, as in patients suffering from typhus fever and especially in patients suffering from cancer of the stomach. These observations, owing to their great practical diagnostic significance, marked an epoch. In the following decade attention was focused chiefly on the clinical relations of ventricular secretion, and a number of researches on this subject were published from the German clinics.

In 1882 Reichmann in Poland described hypersecretion of the gastric juice (gastrosuccorrhea) and in 1885 Rossbach described intermittent hypersecretion. During the years 1884–86 Riegel and also v. d. Velden distinguished between hyperacidity and hypersecretion, continuous or paroxysmal. The enquiry into the motor function of the stomach which had been undertaken by Leube was continued chiefly by his young disciple, Ottomar Rosenbach, who published his results in his well-known paper in 1878. In this paper, for the first time,



ADOLF KUSSMAUL
[1822-1902]

the new investigations concerning the functions of the stomach were viewed in their broader aspects, and were considered to indicate the inauguration of an entirely new movement in clinical medicine. This publication, therefore, deserves to be mentioned at greater length.

Ottomar Rosenbach, then twenty-seven years old, was a true child of German physiological medicine. He was primarily a disciple of Cohnheim and of Traube, the latter being also his near relation. Generally speaking he was more a philosopher than a clinician, more a lover of argument than an observer. His numerous papers are indeed so burdened with philosophical reflections that one reads them with difficulty. This was undoubtedly one of the causes of the comparatively ungracious reception which was accorded to his literary work during his lifetime. Nevertheless he has had a great influence on modern clinical medicine, primarily in Germany, but also wherever centers of scientific clinical work have existed. His peculiar power consisted in enriching clinical medicine with valuable new concepts, new catchwords some might call them. For instance, in the paper of 1878 which we have just mentioned, he introduced the term "ventricular insufficiency" analogous to the term "cardiac insufficiency," a phrase which had recently been introduced by v. Dusch. His aim was to replace the purely anatomical notion of ventricular dilatation, which had previously been held, by a physiological concept. The idea he wished to convey by the term "ventricular insufficiency" was a disproportion between the muscular power of the stomach and the amount of work demanded of it. He considered it important.

Die Medizin, soweit es berechtigt ist, von der Selbstherrlichkeit der pathologisch-anatomischen Betrachtungsweise zu befreien. Uns muss es, da wir heilen wollen, darauf ankommen, nicht einen irreparablen pathologischen Zustand zu diagnostizieren, sondern das Entstehen des Leidens, den Beginn des Prozesses, die Functio laesa des Organs frühzeitig zu erkennen, und darum müssen wir auf die Funktionsprüfung den Hauptakzent legen.

According to Rosenbach it is not by ascertaining anatomic alterations in an organ but by testing its functions physiologically that information is obtained of the first stage of an affection. The behaviour of the stomach can be investigated by introducing a test meal, consisting of a definite quantity of food, such as was proposed by Leube, or even, under certain circumstances and for definite reasons, indigestible food, such as dried berries. Later, after a fixed interval, the stomach is emptied and contents studied. Gastric insufficiency which may be of various degrees may then be detected and studied. By exceeding the functional limit of the expelling motoric force, one creates a *relative insufficiency* of a stomach which may be perfectly able to cope with a less exacting task; but if the stomach is permanently overworked this relative insufficiency sooner or later will develop into an *absolute insufficiency.* In succeeding years Rosenbach described intestinal insufficiency in cases of intestinal stenosis. He also sought to demonstrate an insufficiency of the glandular apparatus of the gastro-intestinal tract which he thought sometimes occurred in certain forms of albuminuria, in diabetes, in obesity and other metabolic disturbances, conditions which were attributed by him to such processes as defective oxidation, defective action of the kidneys or of the pancreas.

In connection with the conception of insufficiency, Rosenbach introduced the term "latent reserve force" of the organs, by which he meant the force which comes into play when the demands upon the organs become greater than normal. He demonstrated this force primarily in the case of the heart. This demonstration was made in connection with his experiments on the artificial production of valvular diseases, carried out under the stimulus of Cohnheim (1878). During these experiments he produced insufficiency of the aortic valves by creating a traumatic lesion. Under these circumstances he found that the heart maintained the circulation without interruption just as before, and it did this because it was able to utilize its reserve force. He thought he could demonstrate similar reserve forces in all other organs, or at any rate, show that they were probably present. He held that in order to judge of the condition of any organ it is, above all, necessary to estimate accurately its functional capacity; it is not enough to ascertain whether gross anatomical alterations are present which interfere with its activity. Moreover, diminished power of work or increased strain on the organ must be demonstrable at an early stage in the development of a malady. In other words, tests are required by which functional power may be measured; methods of *functional diagnosis* must be established. In a little book, "Grundlagen, Aufgaben und Grenzen der Therapie," published in 1891, Rosenbach expanded his ideas, pointing out more particularly the significance of functional diagnosis in relation to therapy.

The diagnosis of the disturbances of the tissue of the diseased organ which is aimed at by the predominant pathologico-anatomical school furnishes the systematician with an apparently convenient classification of the diseases, but it causes the greatest difficulties to the person who is to cure the diseases as it only indicates the rough changes in the tissues, *i.e.*, the permanent changes. But in chronic diseases it must above all be the object to recognize the disease in its very first stage, *i.e.*, the incipient functional disorder.

Rosenbach, as has been said, distinguished, therefore, between relative and absolute insufficiency. The former is curable; it may roughly be said to correspond to exhaustion, or fatigue of the organ; the latter is associated with changes in the chemical or physiological texture of an organ, with or without compensating hypertrophy or its equivalent.

We must not wait, therefore, till permanent dilatation of the stomach or heart has developed, or paralysis of the intestines has occurred, since "*wir heilen und nicht klassifizieren wollen.*" Our aim must be to recognize insufficiency, that is to say, a state in which there is disproportion between the demand made on an organ and its ability to perform work.

To demonstrate insufficiency of this sort new methods are required, methods by which the working capacity of organs, acting under physiological conditions and with a definite output of work may be measured. The stomach is investigated by means of a test meal, the heart by a certain amount of muscular work, the glands by examining the metabolic processes.

The object is to develop a new form for diagnosis, which might be called the functional as opposed to the anatomical form. Functional diagnosis aims at discovering the genesis of the disease, at recognizing the transition from fatigue to disorder of the tissues. By demonstrating incipient morbidity and lessening the demands on the diseased organ we may achieve a cure which would be impossible when permanent changes in the tissues have set in.

The views thus advocated by Rosenbach, and already developed in his first paper in

1878, gained wide approbation. While Kussmaul and his disciples were content to regard functional gastric anomalies merely as the signs of organic diseases in the stomach, such as cancer, ulcer and gastritis, Riegel was instrumental in introducing another view. To his mind hyperacidity and hypersecretion are independent secretory anomalies; they occur so frequently in patients with ulcer or ventricular dilatation because these affections are caused by these disorders in secretion, the secretory disturbances being the primary phenomena of the affections. Thus functional disorders were raised to the dignity of independent morbid categories, to disease entities. The symptoms of these disorders were described, their course and complications. When a functional disorder was diagnosed, the matter was allowed to rest, and the treatment was adjusted to the conditions observed, no further energy being expended in determining or conjecturing what the cause of hyperacidity, or hypersecretion in each case might be.

Beside secretory disorders the various kinds of motor disturbances were also studied. Two distinct degrees of motor insufficiency, the first and second degrees, were described by Boas. These affections, especially the milder form, the so-called atonia ventriculi, were looked upon as primary functional disorders. Originally cessation of the secretion of hydrochloric acid in the stomach had been regarded as a sign of cancer or ventricular atrophy (Ewald). Einhorn later introduced the term of "achylia gastrica" (1892) to indicate a primary "nervous" functional disorder. This phrase was later elaborated by Martius in his book on achylia gastrica simplex (1897) and was elevated to the position of a congenital affection, a constitutional anomaly like color-blindness or hemophilia and the like.

Not only had a series of functional diagnoses been substituted for the purely symptomatic categories which still played a rôle in gastric pathology, under the name of dyspepsia and the like, but the old anatomical diagnoses had been practically discarded. This change in attitude affected cancer least of all, for it was difficult to disregard this entity, but it became the custom to employ the diagnosis "gastric ulcer" only when absolutely necessary. But most of all this point of view affected the use of the term gastritis, which from having been accorded the position of a dominant disease, disappeared almost entirely from clinical, medical nomenclature.

By instituting tests for functional capacity and making diagnoses based on these tests, a series of concepts of functional disease were created, that is to say, pictures of disease, indeed, one might even say functional diseases themselves. These were what one looked for at the bedside; on these one founded one's therapy. The original idea of Rosenbach that the method of functional diagnosis might reveal the incipient stages of disease did not remain the leading thought in this movement. It was succeeded by an attitude of exultation because the pathologico-anatomical point of view had been superseded by the physiological. But since it was obviously necessary to work in the light of categories, a physiological classification was introduced and this was found to be more modern and attractive than the traditional anatomical classification which, from its very nature, seemed to preclude the possibility of successful therapeutic interference.

In analogy with what had been accomplished in regard to gastric conditions, Rosenbach sought to extend and develop functional diagnosis in regard to other organs, and to employ the terms relative and absolute insufficiency in connection with organs other than the stomach. This he attempted primarily in the case of the heart. Like the stomach, this is a muscular organ; its only function is motor, that of causing the blood to circulate. To establish functional tests and to make diagnoses on that basis at first appeared to offer no difficulties; experience, however, proved this view to be incorrect.

The soil had already been prepared for the introduction of this point of view concerning the heart, for the concepts "cardiac insufficiency" and "cardiac failure" had already been employed. The Dublin clinician, Stokes, in 1854, was the first to describe the heart failure which is common to most forms of heart disease as "weakness or deficient muscular power of the heart." The same general idea was expressed almost simultaneously by Beau in Paris (1856) but in a more complete and lucid manner. He called the complex of symptoms engendered through heart failure, *asystolie* and defined it as *une insuffisance de la systole du coeur.* Instead of the French term *asystolie* v. Dusch introduced into German

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[1804-1878]

medicine in 1868 the term "cardiac insufficiency," a term which Rosenbach made popular and which was made, by him and by other German clinicians, chiefly Krehl and Jürgensen, the leading concept in the clinical study of heart disease in the following decades.

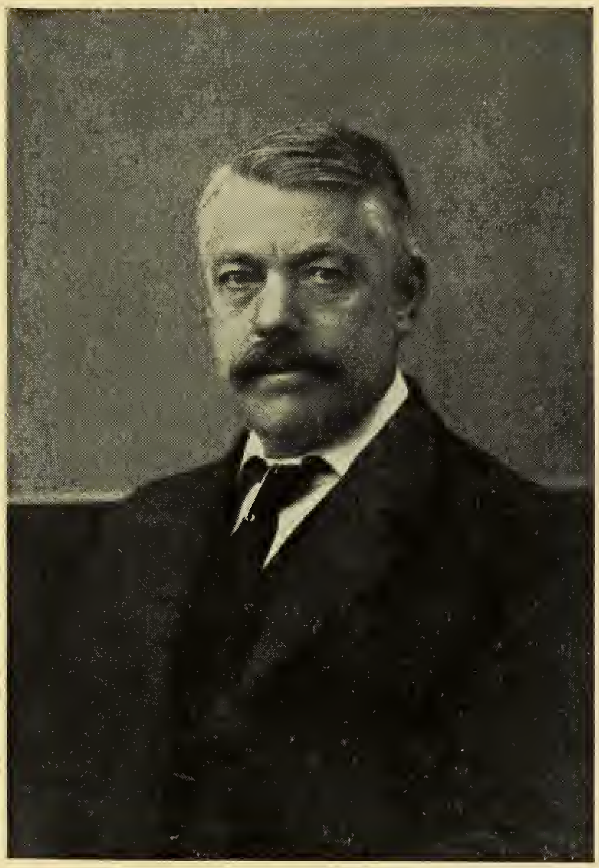
Rosenbach says:

> In heart disease, for instance, it is not the object of the physician to determine the nature of the muscular affection of the heart (fatty degeneration, myocarditis, etc.) but solely to determine the muscular efficiency. The statement formerly so common that a definite affection of cardiac muscle is present and that it is characterized by definite pathological anatomic changes is superseded more and more by the statement that the difficulty resides in insufficiency of the muscular power of the heart.

Disorders of the circulation are in themselves evidence of insufficiency of muscular power of the heart, but attempts to demonstrate insufficiency by functional tests, especially in the milder stages of insufficiency, or accurately to measure varying degrees of insufficiency, present great difficulties. Rosenbach recommended as a test of insufficiency, that patients perform a certain definite amount of muscular work and that the effects of this on the pulse, respiration and general circulation be noted. Later the attempt was made to prescribe accurately the amounts of work to be performed in terms of walking, running, mounting stairs, climbing mountains, through the use of variously constructed ergostats, by cycling, etc. It proved impossible, however, to ascertain the extent of incompetence numerically by this method; only the roughest estimate could be obtained, since so many factors affect the result, chiefly psychic influences, but also the varying condition of the peripheral vessels and so forth.

The attempt was then made to obtain better results by including the measurement of blood-pressure in the investigation. Through the work of the physiologists, Ludwig and Marey, the measurement of blood-pressure had become an important enquiry in physiology. Through the work of Basch and Potain, and later through the studies of Gärtner, Riva-Rocci and Recklinghausen measurements of blood-pressure in patients had been made possible. It was now actually proved that by measuring the increase and decrease of blood-pressure during and after the performance of muscular work, differences could be demonstrated between the behaviour of sound and of diseased hearts, but it proved even more difficult to draw inferences as to the efficiency of the heart from these observations than it was from the investigations of the pulse and respiration. These methods have, therefore, found no lasting favor in clinical medicine in spite of all the work expended on them. The name of the late Klaus Hanssen, a Norwegian clinician, should also be mentioned in connection with these experiments concerning functional capacity of the heart. In all these studies, as Peter F. Holst has pointed out, no true measure of the working power of the heart in patients was obtained. The only result arrived at was a knowledge of the ease or difficulty with which acute failure of the heart could be produced. This production of heart failure, however, is a result that should have been avoided. Nevertheless, the endeavors to find methods for determining the working capacity of the heart in patients were continued. In recent years Sahli has attempted to determine the amount of blood flowing through the radial artery at each pulse beat by means of his sphygmobolometer. The method has not, however, been generally adopted.

Far greater importance must be attached to another movement, in which a quite different method of approach has been employed in the attempt to arrive at an understanding of the functional disorders of the heart. This study was initiated by the physiologists and is intimately connected with the modern development of knowledge concerning the respiratory function. The movement was inaugurated by the energetic work of the Danish physiologist, Bohr, and has later been continued, chiefly by his many disciples. Bohr himself made one of the most important contributions to this subject in his attempt to develop functional diagnoses of the morbid condition of the lung. In the middle of the nineteenth century the study of the function of the lungs was advanced when Hutchinson in England invented the spirometer (1846), and with this apparatus determined the vital capacity of the lungs. Numerous investigators after him applied spirometry to the study of various lung diseases, more especially to tuberculosis. Compared with the importance of the stethoscope, and later of the roentgenogram, in



CHRISTIAN BOHR
[1855-1911]

the diagnosis of lung diseases, this method has occupied a subordinate place. After Panum's work in 1868 on the "vital middle position of the lung" little attention was given to the problems of lung measurement until Bohr in 1906 published his researches on "the vital middle position of the lung and its functional significance."

A series of investigations on this subject now saw the light in Denmark and abroad. Bohr himself came to regard measuring the middle position of the lung as rather important, and considered its variation as a regulatory mechanism of the organism. The study of this regulation and of its abnormalities had, he thought, importance in pathology in general, and more especially for an understanding of heart disease. "The middle position seems actually able to serve as a measure of the functional capacity of the heart," says Bohr in a later publication. Even if this has not proved true, Bohr's investigations, as pointed out by Rubow, aroused a greater interest than had hitherto existed in the pathological significance of the pulmonary circulation. Work in this field is not yet complete; it has recently been taken up in

America by Peabody and by Van Slyke and Lundsgaard.

Of considerably greater value in an investigation of the work of the heart than the examination of the capacity of the lungs are the experiments made by Krogh and Lindhard to determine the quantity of blood flowing through the lungs within a certain time, and on this basis to determine the minute output and the output per beat of the heart. It is obvious that in determining the quantity of blood flowing through the heart in a minute the most accurate measure possible of the work performed by the heart at that time is obtained. While Krogh and Lindhard employed the method worked out by themselves chiefly in physiological enquiries, Lundsgaard applied it in patients suffering from heart disease, and in this way was able to measure the degree of heart failure in valvular disease, and in certain forms of arrhythmia.

Another method of judging of the functional power of the heart was advocated by Kraus, namely, that of measuring the amount of oxygen in the venous blood and employing this information in making a quantitative expression of the state of the whole circulation. His methods, however, were imperfect and the results without great importance. Continued and exceedingly valuable enquiries along this and analogous lines have been conducted by Morawitz and Roehmer, and especially by Lundsgaard who employed methods of blood-gas analysis developed by Van Slyke. These investigations have added important information concerning the functional power of the heart under normal and morbid conditions, but a wide field is left for further enquiry. Meanwhile these studies have been most important in the study of normal and pathological physiology. From the particular viewpoint of clinical study, however, with which it is the special purpose of this paper to deal, the results have as yet had comparatively slight significance. They have not led to the possibility of making functional diagnoses at the bedside analogous to those which can be made in diseases of the stomach. In determining the functional power of the heart in a patient at a given moment no very great advance has been made since the days of Stokes and Beau, or, at any rate, since the time of Rosenbach. Nor have these researches led to the establishment of conceptions of functional diseases of the heart. But the road is now thrown open and is full of promise.

Along other lines, however, progress has been made which has led to results of great and immediate importance in the functional diagnosis of heart disease. Chief among these is the modern investigation of the arrhythmias of the heart. This study was introduced apparently in an attempt to determine the functional capacity of the heart by investigating the behavior of the pulse. From the time of the ancients the state of the pulse has, as we know, been the chief method of estimating the condition of the heart.

After Marey introduced his methods for the graphic registration of the pulse, numerous investigations were made by means of the sphygmograph, but the results were unimportant. It was only when Mackenzie introduced (1893) the polygraph which registered the pulse of the veins and arteries simultaneously that the enquiry gained importance. One of the chief causes of this great advance must, however, be sought in the recent evolution undergone in the study of the normal physiology of the heart under the leadership of Engelmann in Holland and of Gaskell in England. On the basis of their investigations Wenckebach and Mackenzie founded the present knowledge of a series of rhythmic disorders in the functions of the heart. This knowledge was further developed after Einthoven, a Dutch physiologist, worked out his electrocardiographic method for the examination of the heart, a method applied clinically chiefly by Thomas Lewis. A number of clinicians everywhere have worked strenuously in this field. The result has been, in the first place, a more thorough understanding of the construction of the heart and of the mechanism of the heart beat under normal and abnormal conditions; but also the recognition, exceedingly important in the clinic, of a series of well-marked functional disorders such as extrasystolic arrhythmias, auricular fibrillation and the completely irregular pulse, partial and complete heart-block, and paroxysmal tachycardia. The history of the development of our knowledge concerning these functional disorders is similar to that which took place in the case of functional disorders of the stomach. Little by little the several irregularities have been raised to the dignity of functional diseases, perhaps more accurately described as entities of disease, the causes, symptoms, course and treatment of each of which may be studied and described as in the case of other independent "diseases."

The kidneys were next studied from the point of view of functional diagnosis. In respect to these organs also, recent decades have witnessed an exceedingly comprehensive series of investigations in which clinicians and physiologists have worked hand in hand. A survey of the line of development in this instance is also of interest for the better understanding of the tendencies in modern clinical science. In earlier times, from the days of Cotugno and Bright, the chief functional disorders known in affections of the kidneys were albuminuria and edema, and to these were added, by Traube and others, concomitant affections of the heart, especially hypertrophy of this organ. In these abnormalities there was, however, no possibility of measuring the degree of functional disability. The first important step in the modern sense towards instituting a functional investigation of this subject was made in 1897 when v. Korányi's works on osmotic pressure in the blood and urine appeared. By measuring the molecular concentration in these fluids, chiefly by means of cryoscopy he obtained a measure of the power of the kidneys to increase the molecular concentration of the urine, that is to say, a measure of one of the chief functions of the kidneys. From this starting point highly developed methods of diagnosis were very soon evolved, founded on the determination of the physical condition of the urine and the blood.

By the physical methods applied by v. Korányi, cryoscopy and the estimation of electrical conductivity, information was obtained concerning the capacity of the kidneys to secrete solid substances. A frequent phenomenon in diseases of the kidneys was found to be loss of power to secrete concentrated urine, a condition which v. Korányi termed "hyposthenuria." When hyposthenuria was not compensated by the secretion of an abnormally ample quantity of dilute urine, the secretion of metabolic products became imperfect, and insufficiency of the kidneys supervened. This was dependent both on deficient secretion of salts, and on an insufficient secretion of water. It soon proved necessary, however, not to rest content with an examination of the total solid substances secreted by the kidneys, but to distinguish between nitrogenous substances, more especially urea, and mineral substances, more especially sodium chloride, since each of these was found to act quite differently. It soon became the predominant view that it was not so much the quantities of the substances eliminated as it was the retention of these substances in the system which was the sign and measure of insufficiency of the kidneys.

Of urea it had been known since the days of Bright that it accumulated in the blood in cases of uremia. Now it was ascertained (Strauss, Berlin, 1902) that increase in blood urea (or more correctly residual nitrogen) was a frequent phenomenon in patients suffering from kidney diseases and an important sign of insufficiency of the kidneys, even before symptoms of uremia were observed. Widal, in Paris, and Strauss then showed (1902) that there was a direct connection between the retention of sodium chloride and the formation of edema, and that edema might actually be produced by giving sodium chloride to patients whose kidneys failed to secrete it satisfactorily.

By these methods several types of insufficiency of the kidneys were successfully distinguished. The attempt was now made further to develop the diagnosis of these disorders by introducing certain tests designed to demonstrate the capability of the kidneys (*Belastingsprüfung*) in patients suffering from affections of these organs. A water test was introduced as a measure of the power of the kidneys to secrete dilute and concentrated urine. A test of "variability" of this kind was first recommended by Klaus Hanssen and Backer Groendahl in Norway in 1903, and improved later by Strauss and others. The power of secreting sodium chloride was also tested by administering a certain dose of sodium chloride and noting the time of its appearance in the urine, and the power of secreting nitrogen was tested by giving a certain dose of urea and measuring the amount recovered.

A still better way of learning the capacity of the kidneys to secrete nitrogen was, however, at hand in the determination of the residual nitrogen in the blood. The methods for estimating this amount were, however, troublesome and only to a slight extent applicable in the study of patients because a fairly large quantity of blood was required to be withdrawn for the examination. Great improvement took place when the Scandinavian scientist, Ivar Bang, recently, but too prematurely, deceased, developed his special microchemical methods, through which the quantitative analysis of minute quantities of blood has been facilitated, at any rate in respect to its more important components. In this manner it became possible to determine the residual nitrogen in patients and an important method of estimating the functional capacity or insufficiency of the kidneys gained.

About the same time that v. Korányi introduced the freezing-point method, Achard and Castaigne in France initiated another kind of functional test for the kidneys by administering methylene blue and noting the time of its appearance in the urine. The degree of delay in its secretion compared with the normal time of secretion was thought to provide an estimate of the functional power of the kidneys. Instead of methylene blue, a series of other substances have since been used, such as rosanilin, indigo carmine, uranine and most recently, phenolsulphonephthalein. It seems to be true of them all that they can indeed be used for demonstrating disease of the kidneys. For this purpose they are, however, virtually superfluous. But to determine the degree of renal insufficiency they are imperfectly adapted since there is no exact parallelism between their secretion and that of normal metabolic products.

The tests with potassium iodide and lactose, introduced by Schlayer in Germany, gained special importance for some time. Schlayer's procedures were based chiefly on his experimental investigations, as a result of which he thought he could distinguish between tubular and vascular forms of nephritis, special types of the disease which had been set up by Aufrecht. A most important work in this respect has been carried out by Widal and his school. By a series of brilliant clinical researches he has enriched our knowledge of chloride and nitrogen retention, thus creating a systematization of nephritis resting on functional diagnosis, which should supersede the former anatomical division. Principally he differentiated the nephritides into those with chloremia and those with azotemia. To these types of nephritis he joined a third one with arterial hypertension and also described hybrid forms showing at the same time two or three of the functional disorders mentioned. The symptoms and the prognosis of these types were then subjected to a thoroughgoing investigation. In this way a functional conception of kidney disorders was reached, as was already the case in diseases of the stomach and heart.

An enormous amount of work has been performed during recent decades in all civilized countries further to develop the methods for functional diagnosis of the kidneys. The attempt has been continued to arrive at an estimate of the functional capacity of the kidneys by loading tests. Besides trying to demonstrate insufficiency of the kidneys, its degree and different forms, the elaboration of purely functional pictures of disease has been continued.

In other fields of clinical medicine an effort has likewise been made to introduce the use of functional tests, as for instance, in the metabolic disorders. In a general survey of functional diagnosis by Rosenbach (1891) he laid much stress on this subject and raised the question how an incipient insufficiency in metabolic capacity can be recognized. Insufficiency may, in his opinion, be demonstrated partly by abnormal excretion of unassimilated substances, partly by abnormal deposits of fat. The degree of insufficiency is measured by fixing the limit of tolerance for the sub-

OTTOMAR ROSENBACH
[1851-1907]

stance which has been administered. In accordance with this method the amount of carbohydrates tolerated by diabetic patients has long been measured by supplying varying amounts under the same external conditions. This method of measuring degrees of insufficiency has been developed especially by Naunyn and his disciples, and by F. M. Allen at the Rockefeller Institute. The latter has gone further in the same direction by determining the tolerance for carbohydrates in diabetic patients on a diet of pure carbohydrates and by ascertaining the relation of this tolerance to total assimilation. This method has not, however, revealed an association of insufficiency with any single organ; it is the assimilating power of the whole system which is measured, although knowledge has gradually been gained concerning the significance of several organs in the metabolism of sugar, such as pancreas, liver and endocrin glands. In each separate instance, however, we are still ignorant in regard to which organ or what function we are actually testing.

This defect in knowledge is still clearer if we wish to determine the tolerance of the system to given amounts or kinds of nourishment as determined by the larger or smaller deposition of fat. After it was discovered that the deposit of fat can to a great extent be regulated by the glands of internal secretion, such as the hypophysis and the sexual glands, the question has become exceedingly complicated and far removed from solution. The situation, as far as the glands of internal secretion are concerned, is that for the present only the grossly obvious results of their excessive or deficient action can be observed. Characteristic symptom-complexes such as myxedema, exophthalmic goiter and acromegaly resulting from glandular deficiency or overaction are known, but functional capacity of the glands cannot yet be accurately estimated by any known test. The same may in the main be said of the liver, of which only quite subordinate functions can be measured, such as its power of transforming the urobilins. But work in this direction is still being carried on and a great number of experiments are being made with the object of establishing criteria for functional diagnosis in the case of all these organs.

As a very important step in this direction must be reckoned the recent research on basal metabolism elaborated principally in the United States by Graham Lusk, Dubois, etc. The problem of basal metabolism was in the first instance taken up by the German physiologists of Voit's school, particularly Rubner, also by the clinicians, Fr. Müller and Magnus-Levy, who in 1893 and 1895 were the first to demonstrate alterations of the basal metabolism in thyroid affections. The elaboration of indirect calorimetric methods that may be applied at the bedside, has nowadays created a clincially useful functional test; this already has proved to be most important for studying thyroid disorders and as a control of the efficacy of their treatment as practiced to a great extent, *e.g.*, at the Mayo clinic.

If we take a retrospective view of this important movement, it becomes clear that the programme pursued by physiological medicine has consisted in ascertaining functional disorders of organs and employing these disorders as central points in the description of morbid pictures. The methods of experimental physiology have been adopted and employed in clinical research. It may, indeed, be said that with the introduction of functional diagnosis the experiment became the method of clinical examination. If with Claude Bernard we define the experiment as *une observation provoquée,* clinical medicine, by employing loading tests in functional diagnosis, entered into the world of experiment. Clinical medicine thus became more firmly wedded than ever to physiology, and its old love, pathological anatomy, was forced to recede into the background. But with this transformation in methods the importance of etiological factors became secondary and interest in specific disease declined. Functional deviation from the normal came to dominate diagnosis.

In other ways, too, functional diagnosis carried out the ideas of the older physiological medicine. Wunderlich had already proposed that the object of medicine was to diagnose and treat the disorders found in each separate case solely on the basis of the disturbances presented by the individual patient. It was his idea that a case should not be classed merely under a certain heading, placed in a certain fixed category of disease and then treated according to a prescription attached to this category. During Wunderlich's time, however, this programme of individual diagnosis and treatment could not be carried out, as all means of doing so were lacking. With the introduction of functional diagnosis, however, the required methods for diagnosis of transient functional disorders and their degree were provided. By examining the functional capacity of diseased organs and establishing the degree of their insufficiency, information as to the condition present could now be gained which observation of the subjective symptoms alone could give only imperfectly. In searching for means to deal directly with these transient functional disorders, an individual therapy was developed, a therapy of far greater importance than the purely symptomatic, palliative therapy with which the old physiological school was obliged to be contented. These ideas one finds expressed over and over again by leading clinicians whose chief study was functional diagnosis.

How much more important Rosenbach considered it to ascertain the functional capacity of the heart than to examine the actual cardiac lesion in heart diseases has already been mentioned. The same thought was expressed more cautiously and lucidly by Romberg in his textbook on heart disease (1906):

> We do not consider the mere placing of the disease in this or another column as the ultimate purpose of diagnosis. That is only the

necessary premise. The more important thing is to determine to what degree each single patient is injured by his complaint, and what cause has produced the momentary disorder.

In the preface to a book by his two pupils, Kœvesi and Roth-Schultz, on insufficiency of the kidneys, v. Korányi says among other things:

> A fruitful source for therapy springs from our knowledge of the changes taking place in the functions of diseased organs, and of the consequences and dangers to the whole system resulting from insufficiency of individual organs, as well as from our knowledge of the protective measures against insufficiency, or, if it is already present, from the measures suited to fighting and overcoming the consequences of insufficiency and of rendering it harmless. In the continued development of methods looking to these ends and in the art of applying correctly, weighing justly, and combining them wisely, we still have the most urgent of the problems which clinical research has to solve.

In one respect, however, functional diagnosis did not fulfill Rosenbach's expectations. It was his opinion that by its aid the functional disorders of an organ could be diagnosed at an early stage before any lasting anatomical changes had occurred. He hoped that disease might be recognized in its incipient stages and that the morbid process would then be easily accessible to treatment. But this anticipation was realized in a few cases only. How a disturbance develops and to what degree it becomes accessible to treatment depends above all on its cause and is much less dependent on anatomical changes than Rosenbach seemed to think. Even gross anatomical changes may disappear by treatment if they are due, for instance, to syphilis, while even an early and slight functional disorder may be inaccessible to therapeutic influences if it is due to a progressive process such as cancer. It was the complete lack of consideration of the etiology of disease processes and of the fact that the inevitable course of the disease depends upon the etiology which led Rosenbach astray. Generally speaking, this was the weak point in the new physiological movement as it had been in the old. In spite of the enormous advances made in clinical medicine by employing functional diagnosis, the one-sidedness of the underlying principle has led clinical medicine wrong on some important points and has caused checks in progress and occasionally even retrogression.

This has been particularly conspicuous in the domain of gastric disease. This was the field in which functional diagnosis was first introduced, but it was also here that the reaction against purely physiological concepts first made itself felt. The movement is best illustrated by a consideration of the course of prevailing concepts regarding gastric ulcer during this period. What occurred shows the dangers of relying exclusively on functional diagnosis. Gastric ulcer was set up as a special morbid entity by the French pathological anatomist and clinician, Cruveilhier (about 1830). In the following decades it was further studied on the principles of the French school with observation of the characteristic symptoms, chiefly pain and the vomiting of blood, and investigation of the anatomical changes in the stomach. The reader is reminded, at this point, how With in Copenhagen (1881) by faithfully observing the subjective and objective symptoms of patients and correlating them with the anatomical findings arrived at the opinion that gastric ulcer was a much more frequent and important disease than had hitherto been imagined.

When observation of functional behavior became more and more universally employed, and hyperacidity and hypersecretion were to be found associated with ulcer, it was v. d. Velden's first thought that in these abnormalities there had been found diagnostically important signs of ulcer. When, however, Riegel and others came to regard the increased secretion itself as a primary morbid process and to consider ulcer as its consequence, the characteristic symptoms of ulcer were gradually transferred to the newly established morbid picture, "hyperacidity"; gastralgia came to be regarded as a phase of the "hyperacidity trouble," and the clinical peculiarities of ulcer were lost sight of. Gastric ulcer was more and more rarely diagnosed, especially in German clinics, and was considered a possibility only when severe hemorrhage or strictures necessitated it. This movement spread to all countries so that, in effect, ulcer, from having been recognized frequently, came to be a comparatively rarely diagnosed disease.

The reaction came when ulcer began to be treated surgically. Abdominal surgery provided a new method of observing anatomical changes in organs which had previously been accessible to observation only at post-mortem examination. Now the old anatomico-clinical diagnosis was revived. It was the French internist, Soupault, who in 1901 in conjunction with Hartmann, the surgeon, made the important observation that hypersecretion (as described by Reichmann) and the other symptoms usually accompanying it—especially late pains, hunger pains—were always or virtually always due to chronic ulcer. This observation was quickly subscribed to by French clinicians. Starting with this theory clinicians far and wide began to revise their views. The result was that functional disorders were dethroned from the position of primary morbid entities and reduced to their proper place as simple consequences of the important morbid processes which had long been known in gastric pathology. Clinical study in Denmark took an important part in this movement. Rubow, Alf. Madsen, Sk. Kemp, Faber and others showed exactly how the proper kind of study of secretory and motor disturbances might lead to the reconstruction of the nosography and diagnosis of ulcer, and might thus result in improvement in medical as well as in surgical therapy. In other countries a similar movement is on record. In England Moynihan, basing his views on experience gained in many operations, made a great sensation by contending that the condition which the English, following the German example, had called hyperacidity, was in reality a sign of chronic ulcer. Apparently the English had settled down comfortably to the diagnosis of hyperacidity and moreover were not overcritical about the importance of demonstrating its presence objectively in all cases by means of test-meals. Moynihan's vigorous representations, therefore, had all the more effect in the English-speaking world. He erred, no doubt, when he thought that the symptoms mentioned nearly always indicated the presence of ulcer in the duodenum rather than in the stomach (he was evidently ignorant of the work of the French school), but his strenuous work to promote the correct diagnosis of ulcer resulted in a far wider use of operative treatment than before, and through this, in greater knowledge of the disease and improvement in its diagnosis. Further progress in the knowledge concerning this condition resulted from the introduction of methods for investigation of the stomach by means of *x*-rays. This method subserved essentially the purposes of anatomical diagnosis; the shape of the stomach and the changes therein caused by the ulcer were directly observed. Recently this method has obtained special importance in that it has in a way become possible to divide this disease into two subdivisions, pyloric ulcer and gastric ulcer proper, the two conditions differing symptomatically, anatomically and functionally.

It is interesting to see how in the investigation of certain organs, the *x*-ray, as a method of anatomical diagnosis, has attained an importance equal to that which the stethoscope enjoys in diseases of the lungs. Through the use of the *x*-ray knowledge concerning diseases of the stomach and of other abdominal organs has been increased, but, in addition, this method has also been the means of adding much information in an anatomical sense, concerning diseases of the heart, the vessels and the lungs.

So far as gastric ulcer is concerned we have now returned essentially to the viewpoint regarding this condition and to the clinical methods of investigation which were recommended by the Laënnec school. The result has been that ulcer of the stomach is once more properly recognized as a frequent and serious disease.

The recognition of the functional disturbance is now regarded merely as of assistance in diagnosis, just as the study of the subjective symptoms is of importance. Functional disorders as definite entities, however, have to a great extent lost their importance in gastric pathology, and functional diagnosis has, in the main, again become subordinate to anatomical diagnosis. The study of functional disturbance, however, has not been rendered superfluous. On the contrary, during this entire movement it has gained fresh and particular importance, but the hope of replacing anatomical by physiological categories of disease in this sphere has not been fulfilled. Functional diagnosis alone can only suffice in a very narrow field. For instance, the functional disturbance called achylia gastrica continues to form an important and well defined functional disorder. The concept is only of importance, so far as prognosis and treatment are concerned, however, if it is known in each case whether the condition is due to cancer or to catarrhal or toxic gastritis.

In the domain of heart disease a similar movement can be demonstrated, but in neither direction has it run to extremes. Here it was early perceived that purely functional diagnoses would not suffice, though Rosenbach asserted that in a case of cardiac incompetence it did not matter to the patient what was the cause of disease; the treatment remained the same. It is true that the immediate therapy directed toward relieving heart failure is in all essentials the same in every case, but the general viewpoint regarding prognosis and development of the condition, and the problem of its etiologic or specific therapy is, as we know, utterly dependent on the question whether the failure is due to valvular disease, to some form of myocardial disease, or is associated with high blood-pressure due to sclerosis of the kidneys. This side of the matter, however, was frequently undervalued in the early days of functional diagnosis, and mistakes were committed similar to those which were mentioned in the case of gastric ulcer.

In the case of renal disease, functional diagnosis led, in the first place, to the demonstration and investigation of the details of renal insufficiency. But this was followed by a subdivision of the various forms of chronic nephritic disease depending upon the particular kinds of functional disorder that were present. For instance, a distinction was made between the form of nephritis in which the excretion of sodium chloride was obstructed and the form in which retention of nitrogen was the chief phenomenon; between the form with increased blood-pressure and that in which the blood-pressure remained normal. But as functional tests were applied more and more and the results correlated with anatomical findings and with the symptoms and course of the disease in patients, confusion, instead of clarity, resulted.

Extrarenal factors were found to play a greater part in the issue of functional tests than was at first imagined. For instance, it was gradually realized that the greatly reduced excretion of water and sodium chloride in patients with edema is not due to deficiency of the secretory power of the kidneys but is the result of a general disposition to edema, whether this be referred to the minute vessels of the tissues throughout the body, or to the tissues themselves.

Under these circumstances the very elaborate and numerous functional tests originally employed have lost some of their value and have, therefore, been simplified. Von Korányi's methods, involving the determination of freezing-point and conductivity, have now been abandoned in favor of a simple determination of specific gravity; the test for sodium chloride has lost a great deal of its importance; and the urea test has been rendered superfluous by the far more important determination of the residual nitrogen in the blood. There is left to us the old test of v. Korányi of the power of the kidneys to secrete concentrated and dilute urine; the test for variability, as it is systematized, for instance, in the Strauss test, and also this test employed in conjunction with the determination of the residual nitrogen.

While a more modest rôle has been assigned to functional diagnosis in its relation to kidney disease, than occurred in the case of its relation to diseases of the stomach, nevertheless the attempt has been made to build up a new nosography for chronic nephritic disease by correlating with the functional disturbances, the more minute anatomical changes, and the clinical course of the disease. Volhard and Fahr's great work "Die Brightsche Nierenkrankheit," in which precisely these classical clinical methods were applied, has been of real significance.

A clue to the modern trend of this subject will be found in a certain passage in the report of the leading German clinician, Fr. Müller, on Bright's disease, made at Meran in 1905 before the German Pathological Society. Its argument is directed primarily against the old pathologico-anatomical school, but the effort is also made to assign functional diagnosis to its proper place.

> In the study of a disease the highest aim cannot be confined to prognosticating at the bedside, with the greatest accuracy possible, the changes which may be found on the post-mortem table. It is more important to seek the *causes* of disease and to start its investigation with the view of ascertaining these. The notion of "morbific cause" has gradually suffered a certain displacement. Whereas in earlier days we were content to conceive the organic changes found at post-mortem examination as causes of the morbid symptoms observed in the living, nowadays we no longer regard these pathologico-anatomical changes in the organs as the ultimate and actual causes, but more as manifestations (*Erscheinungen*) of the diseases on a level with the symptoms observed *intra vitam*, and we seek to disclose the injurious potencies which have led to these organic changes as well

as to the functional disorders connected with them.

The attempt to class and name the diseases according to their etiology and not according to their pathologico-anatomical base has not only proved beneficial in the field of infectious diseases but has *inter alia* given excellent results in the case of heart diseases. It will also be permissible to apply this principle of division to the nephritic diseases; this cannot, however, be carried out with any prospect of success unless it should prove that the nephritic diseases occurring after the various infections and intoxications show special characteristics.

In German clinical research much work has been done during the last decades from this point of view. The attempt to divide from the old clinical group of Bright's disease another series of morbid processes has been successful. The various forms of nephrosis, for example, which were previously combined, in the main, under the head of parenchymatous nephritis, have recently been regarded separately. Here, as everywhere in clinical medicine, it has become apparent that the dictum of Fr. Müller holds good; corresponding to the various etiological entities, there are variations in the clinical manifestations, and the goal, which should be aimed at, is the establishment of sharply defined morbid pictures.

Whenever its intimate connection with clinical observation has been broken, medical science has been led astray again and again in the days of functional diagnosis as in the days of cellular pathology; both times the causes have been identical. In both instances the special objects of clinical research and the methods dependent upon these objects have no longer commanded respect. Formerly it was microscopic cellular anatomy which was allowed to dominate clinical observation, now it was physiological argument and investigations.

There is a signal difference between the physiological and the clinical study of functional disturbances. In physiology the study of the functions of the various organs is an end in itself. Life is comprehended as the sum of the various visceral and cellular functions. If the physiologist encounters changes in the functions of an organ, they enlist his interest chiefly because these functional disturbances teach him something of the general laws applying to the function, revealing to him aspects of activity which were hitherto unknown.

But in clinical medicine the study of disturbance in organs has a widely different import. The main object of the clinical study is first to find what has caused the disturbance in the normal life of the organism, and then to understand how the cause has given rise to that series of law-directed phenomena designated by the name of disease. While the physiologist works back to normal function from the observed disorder, the clinician is primarily in quest of the cause of the disorder; the functional disturbance is chiefly of interest to him as a means to this end. With regard to functional disturbances and possible anatomical changes the clinician is therefore specially concerned to know how the various changes tend to develop; he is interested in following the course and issue of disease. Only through study along these lines can he succeed in describing morbid pictures of lasting value, morbid pictures which represent the total effects of definite injurious agents on the life of the organism. All the methods of clinical research tend more or less consciously towards this goal.

Functional diagnosis was introduced with the watchword "*Wir wollen heilen und nicht klassifizieren,*" but it has shared the fate of all other clinical methods; they all lead ultimately to new classifications, to the dissociation of non-homogeneous processes, and to the consolidation of homogeneous ones.

Indeed through the study of functional disturbance much greater progress has been made in nosography than occurred when pathological anatomy was the only guide. In the first place nosography has been enriched by the addition of the investigation of functions to pure symptomatology. Objective and measurable criteria have been provided which supplement and extend the information obtained through study of the subjective symptoms alone. By correlating functional disturbance with anatomical change it has been possible to advance along the lines indicated by the Paris school. How in the domain of gastric diseases functional diagnosis led to a fresh development in anatomical diagnosis has already been pointed out.

In the second place the investigation of function has greatly contributed to the development of methods for locating the seat of disease. As a rule the demonstration of a disturbance in function is accompanied by a demonstration of the organ which is involved. Through the study of function it is often possible to locate the seat of a disease when the ordinary objective examination does not reveal the anatomical foundation. Through functional investigation it is often possible not only to locate the disease in a definite organ, but also to put one's finger on the particular part of the organ, the particular cells or cellular complexes which have been attacked. Just as this kind of precision has long been possible in the case of diseases of the nervous system, so has it also proved to be possible in certain forms of cardiac disease. For instance, certain affections can now be located in the conducting system of the heart. Indeed since electrocardiography has been employed, it has even become possible to locate the seat of a break in conduction in one or the other branches of the His-Tawara bundle. In the completely irregular pulse the seat of disturbance has been localized in the auricles. In the case of nephritic disease the effort has also been made, through functional investigation, to locate a given disorder in the glomeruli or in the tubules. Even if this attempt has not yet been successful, the way has at least been indicated. One of the aims of functional investigation is thus to arrive at a physiological cellular pathology, analogous to Virchow's anatomical cellular pathology.

Finally, through functional diagnosis, affections, functional disturbances, in organs or cells which never become the seat of anatomically demonstrable changes, can be demonstrated. Functional diagnosis has made possible the description of new morbid pictures as characteristic and independent as those established by means of pathological anatomy. As a matter of fact diabetes mellitus presents an old and classic example of a purely functional morbid entity. And indeed, in a large series of similar functional diseases, such as adipositas and other metabolic abnormalities, orthostatic albuminuria, habitual constipation, migraine, epilepsy and certain other nervous diseases, not to mention most mental diseases, significant anatomical changes have been looked for in vain. All these diseases are partly symptomatic; nevertheless, the endeavor should be made to find a basis for each of these in a morbid change in function underlying the symptoms. Instead of purely symptomatic pictures, pictures of characteristic functional diseases may result. In this way the causes of functional disturbances may ultimately be discovered.

In this connection it is interesting to note that in psychiatry the cause of the various psychoses is now sought in functional disturbances of the endocrine glands. It is further interesting to observe that the modern conception of the acid-base equilibrium of the blood, which is based largely upon the investigations of L. J. Henderson in America and of Hasselbalch in Denmark, is beginning to be applied to the pathology of nervous diseases, more especially to epilepsy and psychoses (Bisgaard and Jarloev in Copenhagen). It is now generally recognized that hope for the solution of the problems concerning functional abnormalities is principally centered in the application of biochemical and biophysical methods.

In the modern clinic, work in the laboratory is so intimately connected with purely clinical work that there can be no great progress without using methods derived from the experimental laboratories. This applies also to nosography. Of course, new diseases can still appear or be discovered in the same manner as occurred in earlier times, as has recently happened, for instance, in the case of trench fever and encephalitis lethargica, to mention two of the newest additions. The bacteriological clinic is still working out new clinical entities, such as Leptospira icterohaemorrhagiae, and is dividing old entities into new ones by subdividing bacteria into different types, as Cole and his associates have done in the case of pneumococcus causing pneumonia, and as others have done in the case of the bacteria causing dysentery and the meningococcus causing meningitis. Steady progress in transforming nosographical conceptions of morbid phenomena is, however, performed chiefly by clinical observation in connection with physiological investigation. For instance, the new and widely spread disease, hemolytic icterus, was not established as an entity until Chauffard in the clinical laboratory demonstrated the diminished osmotic resistance of the red blood corpuscles. The existence of the specific, very "innocent" form of chronic glycosuria, renal diabetes, was only confirmed through a long series of analyses of the blood sugar. Progress in the clinical and etiological classification of certain blood diseases, such as purpura, can only be accomplished by exact counting of blood platelets.

The period of functional diagnosis, with its intensified study with physiological methods of research, has contributed greatly to breaking down the barriers which formerly existed between the experimental and the clinical branches of medicine. The old demand for the same scientific accuracy of method and reasoning in clinical research, as is required in the experimental institute, has now been universally recognized and appreciated. A basis has been established for continuous and fruitful interplay. From physiology, clinical medicine constantly receives new methods for investigating disturbances of function, and the clinic is compelled to follow closely the evolution of these methods. Separation between experimental and clinical research is no longer possible; they are working closely together. A division of the work will, however, always be necessary because clinical research must derive its inspiration from the examination of patients. The manner in which clinical research is carried on in hospitals has been changed. Laboratories have become an increasingly dominating element in the medical clinics, but, whereas in the older physiological medicine they were chiefly used for experiments on animals, they have now proved indispensable in the more thorough-going examination of patients and in ascertaining the nature of the morbid changes in functions. Functional diagnosis has directed the footsteps of the clinician, who is interested in the methods and data of physiology, back to the bedside, where his true kingdom lies.

PART VI

CONSTITUTIONAL PATHOLOGY

The most recent movement in nosography belongs almost entirely to the twentieth century, and is directly associated with the influence which modern research on heredity has had on pathology.

It has long been admitted that heredity is an important factor in the genesis of many diseases, but until very recently this circumstance exerted little or no influence on the development of nosography. When the whole problem of morbific causes was shrouded in darkness, notions concerning the relation of heredity to disease were also extremely vague. In discussing the etiology of a disease, a number of factors were usually enumerated and among them, heredity was frequently mentioned. This factor was, in a manner, made coordinate with other injurious influences, such as underfeeding, chills, grief, overexertion, etc., and the relative importance of the hereditary factors in the etiology of different diseases was believed to be very variable. In one disease it was thought to be of significance in only a few of the cases; in another disease it was believed to play a rôle in half the cases or even more. This point of view yielded nothing to nosography. The part which heredity played in any disease was not sufficiently definite that it could be considered a distinguishing characteristic and so employed in the differentiation and classification of the various diseases.

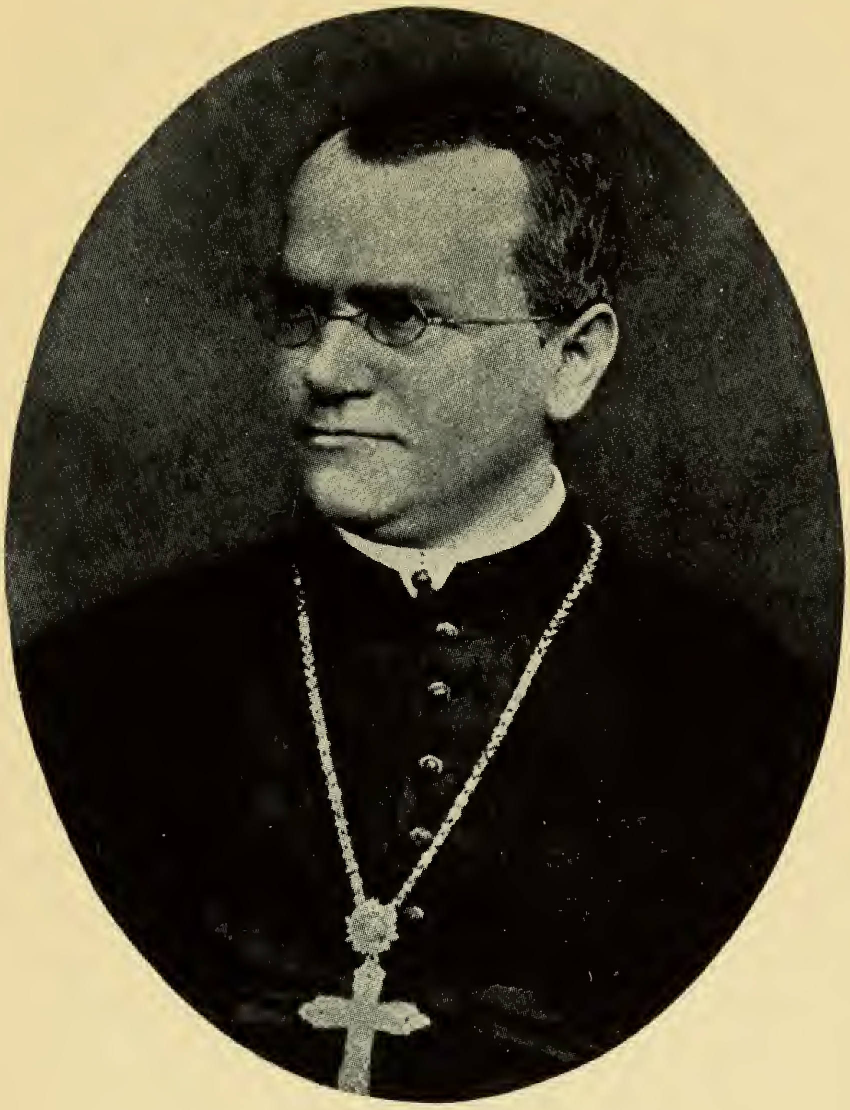
An enormous change has recently taken place in this state of affairs, however, first as a result of the development of newer doctrines concerning infections, and second, and to a much greater extent, as a result of the discovery of new biological laws concerning heredity.

As soon as the doctrine of infection had been generally accepted, the question of the inheritability of infectious diseases was quite naturally taken up for discussion and critical examination. Among the diseases which had always been considered most markedly and plainly hereditary, were some of the most important chronic infectious diseases, namely, tuberculosis, syphilis and leprosy. With regard to these diseases it was very soon ascertained that the heredity here in question depended chiefly upon the direct or indirect transference of infection from parents to children after birth. This kind of heredity should, of course, be well distinguished from other kinds. In his "General Pathology" (1896) C. Lange, the Dane, gives a discussion of pathological heredity which is unusually lucid for the time at which it was written. In this treatise he employed the term "pseudoheredity," to designate the tendency in certain families to suffer from certain infectious diseases, which, as we have stated above, may be explained by transference of infection from parent to child; and he also included under this term the special tendency in certain families to the occurrence of certain other diseases, due to the exposure of the entire family to the same external circumstances playing a part in etiology. Finally he was inclined to include, under the same term, the examples of inheritance of disease which are dependent upon fetal or germinal transmission of the infectious agent. On the other hand, he limited the term "blastogenic" or true heredity to that form of heredity which is associated with organic defects in the generative cells of the parents. In accordance with these views Johannsen later made the distinction between false and true heredity which is current in biology.

The exclusion of all cases of false heredity brought greater clarity to the clinical doctrine of heredity, but of still greater clarifying effect was the development of the whole modern experimental doctrine of heredity with its biological laws of heredity. According to these laws single properties, and hence single abnormalities, delimited morbid phenomena, may be inherited quite independently of the other properties of the organism, and they may be coupled with one or several of these. Through the doctrine of the distinction between dominant and recessive properties an explanation was afforded of the apparently quite capricious and desultory occurrence of certain morbid family peculiarities; through the doctrine of sex-limited inheritance a series of other obscure clinical observations were elucidated. Old observations on the significance of consanguinity, so-called atavism, etc., appeared in quite a new light and the question of the inheritance of morbid phenomena became keenly interesting.

As is well known, it was the experiments of the Austrian, G. Mendel, which about 1865 laid the foundation of the new movement in biology; but his experiments and his laws of heredity remained almost unknown until the laws were rediscovered and corroborated at the commencement of the new century. His observations were later supplemented by de Vries' doctrine of mutation, by Bateson's studies on the coupling and repulsion of hereditary factors, and by Johannsen's work on heredity in "pure lines." Of great importance, too, for the general subject of heredity, but especially, as will be seen, for heredity in medicine, is also Johannsen's introduction of the terms "genotype" and "phenotype."

The discovery of these new facts and laws concerning heredity soon led physicians to review the knowledge concerning so-called hereditary diseases in the hope of applying the new biological discoveries to the study of these conditions. A considerable number of diseases which have been shown to be hereditary are now well known. They include such conditions as hemophilia, which was described as a family complaint as early as 1803 by the American, Otto, and color blindness, Daltonism, which has been known to be a hereditary disease since the middle of the nineteenth century. In addition certain purely anatomical deformi-



GREGOR JOHANN MENDEL
[1822-1884]

ties, such as supernumerary fingers, have long been recognized as hereditary. It was soon found that these morbid phenomena resemble other biological hereditary phenomena and obey the same laws. These diseases, therefore, are of a particular kind; they have a peculiar and characteristic etiology. It was now possible and justifiable to collect into a special nosographical group all these "heredito-familiary" diseases.

We cannot wonder that the English clinicians were among the first to take up the question of these hereditary diseases for investigation and discussion. Since Darwin, the problem of heredity had been a burning question in English science and more recently Galton's well-known investigations and Bateson's book on "Mendel's Principles of Heredity," which was published in 1902, had again made it the subject of general discussion and enquiry. It is not surprising, therefore, that very soon Farabee and Drinkwater were studying finger deformities on Mendel's principles, Gowers, Mott, Savage and several others were investigating the part played by heredity in the field of nervous diseases, while the ophthalmologist, Nettleship, in his publications from 1905 to 1909, set forth the results of his studies concerning the manifold hereditary diseases of the eye.

Not only in England, however, but in all countries, much attention has been directed during the last decade towards finding real hereditary diseases, and as a result a large number of hereditary morbid abnormalities have been added to the fairly long list which had long been known. As soon as the search was undertaken by observant physicians, it became apparent that there existed a whole series of clinically well-defined and well-delimited entities of disease which were only waiting to receive the stamp of a specific etiology in order to take their place as specific diseases. By the clinical nosographical method it had been possible to combine certain groups of cases exhibiting a typical symptomatology and course. This indicated a specific etiology for the group, which was now found to be heredity. For instance, the gifted clinician, Duchenne de Boulogne, as early as 1856 had described, as a special clinical type, infantile muscular dystrophy with pseudohypertrophy, in which heredity apparently played a great part. This has long been regarded as a definite and well-characterized disease clinically, but it is only now, since it has been demonstrated that the essential etiological factor is heredity, that we are justified in considering it a definite morbid entity. At present it is regarded as a particularly well-pronounced example of the familio-hereditary diseases.

Moreover, it became apparent that it was important to observe and investigate the hereditary occurrence of various morbid phenomena and the occurrence and course of the associated symptoms, since by this method it became possible to set up one hereditary disease after another. As an excellent example may be mentioned the important study of myoclonus-epilepsy made by Lundborg, a Swede. The characteristic symptom-complex of this disease had already been described (Unverricht, 1891), but only through Lundborg's comprehensive investigations on the occurrence of the disease in a certain family in a province of Sweden was it ascertained that the disease was a specific hereditary disease, following the Mendelian laws, and occurring more particularly as a recessive character.

In the work of establishing or creating new types of hereditary disease, anatomical as well as functional diagnosis is required, since hereditary diseases of a purely anatomical kind occur as well as those of a purely functional kind, and in addition those of a combined kind.

While as late as 1908 long discussions could still be held in the English Royal Medical Society as to whether the hereditary diseases follow Mendel's laws or not, we can now make up a long list of diseases which undoubtedly follow these laws in their occurrence. As a rule they are dependent upon a dominant factor in one of the parents. In 1917 the German, Dresel, was able to make up a list of 30 hereditary diseases where this had been demonstrated by the analysis of statistics from a large number of cases. On the other hand, he only found certain documentary evidence of a disease as a recessive property in the case of 6 diseases. For 4 diseases sex-limited inheritance has been demonstrated beyond a doubt.

If we take a single organ such as the eye, the number of hereditary diseases known is strikingly great. There occur diseases that are inherited as dominant properties, others as recessive properties, and still others as properties limited to sex, and there are purely functionally hereditary diseases, as well as anatomically hereditary diseases.[1]

That such a comparatively large number of the known hereditary diseases are diseases of the eye is probably due to several reasons. The eye is more accessible to close investigation than any other organ, and every deviation in structure, however slight, is more apparent here than in any other organ, just as every functional anomaly of the eye may be easily demonstrated. As already remarked, the hereditary diseases of this organ are very often of a purely functional nature without any demonstrable anatomical changes. In these instances the disease is characterized only by certain typical functional abnormalities. Nevertheless, these functional disturbances have been demonstrated to have a specific etiology, that is, heredity, and it is justifiable, therefore, to consider them entities of disease.

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[1] Dresel gives the following ophthalmic diseases which are inherited as dominant factors in the ratio of 1 to 1: irideremia, congenital cataract, juvenile cataract, simple hemeralopia, coloboma nervi optici, myopia hereditary ophthalmoplegia, distichiasis; as a recessive property, primarily inherited retinitis pigmentosa, likewise, probably, total color blindness, etc.; as a sex-limited property, inherited Daltonism and hemeralopia combined with myopia.

It is probable that as functional diagnosis gradually joins hands with research on heredity, an increasing number of similar hereditary functional diseases in other organs will be discovered. For instance, there are many only partially recognized abnormalities of the nervous system which may be true disease entities of this character. In the case of the kidneys, diabetes insipidus is such a disease, and recent investigations concerning renal glycosuria, an entirely benignant form of diabetes, indicates that this condition is just such an hereditary disturbance of the secretory function of the kidneys. In many cases an inherited functional disturbance gradually leads to well-pronounced anatomical changes, such as, for instance, occur in the case of hemolytic icterus, investigated in Denmark by Meulengracht. In these fields there is still much work to be done and much new land to be conquered through clinical research. As Nettleship says in his Bowman Lecture of 1909: "There is still virgin ground where the tasks of excavating, collecting and recording may be safely undertaken by those who enjoy them."

The general significance which the investigation of hereditary morbid phenomena bears to clinical nosography is very clearly stated by the Hungarian neurologist, Jendrassik, in his contribution to Lewandowsky's great work on nervous diseases (1912), and his views therefore deserve to be quoted:

> Only with difficulty has the etiological point of view gained acceptance in practical medicine; it was only the obvious conditions as regards many infectious diseases that caused the conception of diseases as etiologically distinct entities to be generally employed as a guide in internal medicine. With even greater difficulty did this view gain admittance in neurology, while psychiatry has had the greatest difficulty in adapting itself to the new ideas.
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> The principle of the etiological specificity of disease implies that every disease entity is produced by a quite particular cause, that different diseases cannot arise from the same cause, nor can different causes produce the same disease. We now conceive of each of the pathological processes as a single, gradually developing phenomenon resulting from the action of the specific etiologic agent, though with variations depending on individual circumstances or external conditions. Symptom-complexes cannot pass for diseases.
>
> On this view the diseases must mainly be divided into two large groups, the first of which comprises the exogenous affections, while the

second group contains the endogenous affections, *i.e.*, such whose cause is some defect in the formation or developing power of the single parts of the organism. The cause of these latter defects can only be an inherited one, as external causes have been excluded.

Such a division of all the diseases into two main groups is very attractive and clear, and has been very generally adopted. Nevertheless, on closer consideration, it is evident that the attempt to apply this classification to every disease involves certain difficulties which are very fundamental in character. For instance, the term "endogenous" has been applied to various affections produced by a morbid state of the endocrine glands, such as obesity or dwarfism associated with disease of the hypophysis. Now it is well recognized that the alterations in the hypophysis may be produced by an entirely exogenous tumor, perhaps even by trauma. This obstacle might without difficulty be overcome by making an exception of these cases and grouping them apart from the really endogenous affections. A more serious difficulty, however, consists in the fact that it is very often difficult or impossible to draw the line between endogenous and exogenous affections. For instance, the common form of shortsightedness develops, according to the current view, chiefly as a result of habitual close work with the eyes, such as reading too constantly or under unfavorable conditions. The condition, however, does not develop with equal facility in all persons; heredity has a great and easily demonstrable influence on its occurrence. Epilepsy is a distinctly hereditary disease, but it may also be caused by a blow on the head or a lesion of the brain. In individuals who are predisposed through heredity, however, trauma or meningitis will more easily produce epilepsy than it will in others. In view of these facts, are nearsightedness and epilepsy endogenous or exogenous diseases?

According to Johannsen's doctrine all disease, all abnormalities must be conceived as parts of the phenotype, and the latter arises through an interplay of the genotype and the external conditions. In some cases of hereditary disease the external circumstances seem to play quite a subordinate part; they follow an iron law of nature, occur with fully law-directed regularity in accordance with the Mendelian laws of heredity and seem entirely independent of external influences. The genotype is entirely predominant. In other words, the "usual" circumstances, in the widest sense,—those under which man is born and grows up, in conjunction with the genotype, make the disease appear, make it part of the phenotype. In other cases certain circumstances, certain external influences, must be present before the disease can appear. The genotype in these cases appears to be merely a predisposition to disease, sometimes a predisposition to certain definite diseases. In this way the problems concerning the inheritance of disease and those relating to predisposition to disease are brought into close touch, and it cannot be a matter for wonder, therefore, that in modern medicine these two problems are dealt with collectively. Together with the subject of general constitutional anomalies they form the theme of *constitutional pathology* which has recently attracted great attention, more especially in Germany. This subject in several respects has an important bearing on clinical medicine, chiefly on account of its relation to the latest phase of nosography.

As a matter of fact, modern constitutional pathology first appeared as a reaction against etiologico-clinical research and the nosography which was founded upon it. In the study of the infectious diseases especially, the etiological point of view had come to be of exclusive interest. But now certain questions arose. What is a cause? Is it justifiable to say that a disease has one cause? Has not disease, like all other phenomena of this world, not only one, but many causes, and is it not more correct to say that the morbid phenomena in each separate case appear as a result of a series of conditions? Indeed, ought we not give up speaking about "causes" in pathology, as we have done in the other physical sciences and be content with speaking of conditions?

These questions began to arise in the minds of scientists very soon after bacteriological investigation had revealed the "actual cause" in a series of important diseases. The first fact which tended to disprove the simple statement that a microbe is the cause of a given disease, was furnished by Pasteur himself. In 1880 he demonstrated in the mouth of a perfectly healthy child a pathogenic microbe, a diplococcus. Later this same organism, pneumococcus, was shown to be the cause of typical inflammation of the lungs, and also of certain forms of brain fever, of heart disease, etc.

It soon became apparent that an analogous situation existed in relation to the etiological agents of certain other infectious diseases. Loeffler found the diphtheria bacillus in the mouth of a healthy individual at the same time that he discovered it on the mucous membranes of diphtheria cases. Cholera and typhoid bacilli were often found to be present in perfectly healthy individuals; the mere presence of tubercle bacilli in the body was not alone sufficient to produce phthisis. Gradually the existence of healthy, but infection-transmitting bacillus-carriers became universally recognized, and it became generally acknowledged that a pathogenic microbe alone was not sufficient to cause a disease. The presence of the organism is a necessary condition, but the organism alone is not the sole cause. The individual must be susceptible to infection and this, again, involves two circumstances. A momentary, local susceptibility due to a wound, a chill, a weakening of the tissues or the like, must be present. But besides this accidental cause or condition, there must also be a general susceptibility, a predisposition. The want of this general susceptibility is what may be called immunity, and it is due above all to the genius of Pasteur that pathology at once devoted itself to this problem in the hope of securing protection for the race against the infectious diseases.

But simultaneously with the development of this interest in immunity there developed an interest in the opposite condition, namely, the predisposition to disease. Attention was directed especially to infectious diseases such as tuberculosis, which attack only a relatively small number of individuals, though the sources of infection are widely diffused. This modern interest in the general predisposition, in the constitution of the organism, expressed itself in the form of direct opposition to the doctrine of specific diseases and specific morbific causes. This is illustrated in an interesting way by a lecture delivered by the German hygienist, Hueppe, at the meeting of Natural Scientists at Nuremberg in 1893: "Über die Ursachen der Gährungen und Infectionskrankheiten und deren Beziehungen zum Kausalproblem und zur Energetik."

In this lecture Hueppe, like the physiological clinicians of the middle of the nineteenth century, raises his voice against Sydenham's conception of the diseases as species, against this *von Zeit zur Zeit aufgewärmten Rest der Ontologie*, but he also opposes the Pasteur-Koch view that microparasites may be regarded as the "cause" of fermentation and of infectious diseases, may even be looked upon as "specific" causes. Contrasted with this very simple point of view he postulates the following:

> The decisive cause of disease and fermentation lies in the structure and disposition of the infected host and in the structure and constitution of the fermentable matter. Only the internal constitution can quantitatively and qualitatively contain everything that appears following the action of the external influence, which thus acts as a release of existing, apparently latent, potential, internal energy.

To illustrate his conception of the manner in which the universally accepted morbific causes induce disease, that is, act as agents which release the latent energy of the organism, he adduces certain examples often used in philosophy, such as the action of the spark which fires the powder. In this case, the cause of the explosion must be sought in the latent energy of the chemical substances concerned. He also mentions the avalanche which is caused to move and fall by some slight accident, such as the flight of a bird, the sound of a voice, or the like. The spark, the sound, etc., are the releasing agents, but the display of energy which takes place is due to the latent, potential energy present. For such potential energy to be released by some external cause, various conditions must be present, and the same phenomena are only released when the same conditions are present. As regards disease, unless proper conditions are present, the specific microbes and cells cease to react specifically.

Therefore, viewed from the only standpoint which is scientifically justifiable, the ontological conception of specific morbific causes and specific infectious diseases is just as untenable as it is superfluous. The nature of specificity is not involved in the specific character of the morbific causes, but resides rather in the uniformity of the external conditions, and no properties in the bacterium are more easily affected than the specific properties themselves.

This being the case, Hueppe cannot any longer look upon specific morbid species, specific cells, and specific microbes as fit subjects for scientific consideration, but he admits that the ontological view may possess certain advantages for beginners. "Like the personifications of the religions, these entities offer certain advantages as transition stages for untrained reasoning, but from a purely scientific point of view they are unacceptable."

On the other hand, he emphasizes the importance of morbid disposition and predisposition. Just as the various sugars have a different chemical constitution and therefore differ in fermentative capacity, so the various families, species and races, as also persons of various ages, members of different professions, etc., are variously predisposed to disease.

How in the presence of such facts anybody can deny the importance of a morbid predisposition as a cause and the inheritance of a morbid constitution, is quite incomprehensible to me, and is only conceivable in a person who has not surveyed the subject scientifically, and because he is still held by the fetters of ontology which do not permit him to view the objects in their various aspects.

It was perhaps necessary to raise a warning against the exclusive study of the growth of pathogenic microbes as it was being carried on by Koch and his followers. As already remarked, the school of Pasteur had devoted itself with the greatest interest to the question of immunity and predisposition. The relation of *le microbe* to *le terrain* was a constant subject of research by this school. Trousseau even touched upon this question of individual susceptibility in his early prophetical prognostications concerning the results which were likely to follow Pasteur's investigations.

The stress laid by Hueppe on disposition to disease has been fully justified by later experience, but his opposition to specific morbific causes and specific diseases was, to use one of his own expressions, "as untenable as it was superfluous." Nevertheless, in the succeeding years, he gained followers in Germany who adopted his opinions on both of these points, chiefly Martius, but also Gottstein, Hansemann and Verworn, and the discussion concerning these philosophical problems raised by Hueppe has been kept alive by these men. The exact nature of this discussion is evident from the titles of some of the papers and pamphlets which have appeared: Verworn, "Kausale und konditionelle Weltanschauung" (1912); Hansemann, "Über das konditionelle Denken in der Medizin und seine Bedeutung für die Praxis" (1912); Martius, "Das Kausalproblem in der Medizin" (1914).

This discussion has been continued up to the present, though recently Lubarsch in concluding a paper entitled "Ursachenforschung, Ursachenbegriff und Bedingungslehre" (*Deutsche med. Wchnschr.*, January, 1919) expresses the hope that in the future, scientists will devote their energies to solving individual scientific problems instead of discussing the complex problem of causality.

It does not seem likely, however, that this will end the discussion. There are indeed some phases of this problem which should still be discussed, for certain concepts which are concerned are used in different places in widely differing senses and important terms are given widely separated definitions. This is especially the case with the terms "constitution" and "constitutional disease."

The term "constitution" has been employed in medicine since the days of the ancients, and at first was used in a very comprehensive and vague manner. For instance, Hippocrates spoke of the constitution of the individual, the people and the country as well as of the constitution of the seasons, the atmosphere and the prevailing diseases. But gradually the term came to be employed chiefly in two connections. Writers began to speak of the "epidemical constitution." This conception of constitution was chiefly evolved by Sydenham and was a further development of Hippocrates' theories concerning the influence of seasons and the weather on the occurrence of diseases.

The other sense in which the term was employed was in relation to the individual, the constitution of the individual, a good or bad constitution, a strong or weak constitution, etc.

This double sense of the word is well illustrated by its use in certain articles by de Montègre, published in 1813, in the well known "Dictionnaire des Sciences Médicales." He mentions here two kinds of constitutional diseases. The diseases of one kind are produced by the metereological constitution; these are the acute and epidemical diseases. Those of the other variety are dependent upon the bodily constitution of the individual attacked. These diseases as a rule are hereditary, but in the great majority of diseases the bodily constitution is of importance. The athletic constitution, for instance, predisposes to acute inflammations, etc. As examples of typical constitutional diseases he mentions phthisis and apoplexy.

In the middle of the century, however, a constitutional disease began to be regarded as synonymous with a general affection which attacked the whole organism, in contradistinction to a local affection. Thus Wunderlich in his "Handbuch der Pathologie und Therapie" (1846–54) devotes a special section to constitutional diseases, and in this class he places the "autogenetic constitutional diseases" (such as anemia, hemorrhagic diathesis, metabolic diseases, gout, diabetes, edema, etc.), and also the intoxications and all the acute and chronic infectious diseases. Syphilis begins as a local infection but becomes "constitutional" when the whole system is infected.

This new conception of constitutional diseases was very soon universally adopted. The doctrine of the epidemical constitution had gradually faded into insignificance and at last almost entirely disappeared. Also the doctrine of the individual bodily constitution receded more and more. On the other hand, the rapid development of anatomical local diagnosis rendered it more and more necessary to provide a category of constitutional diseases under which could be grouped those diseases which could not possibly be regarded as the manifestations of a purely localized condition, and such a group is found in all the textbooks dating from the latter half of the century. Thus Jaccoud, in his "Traité de Pathologie Interne," dating from 1869–71, places the following diseases in the class "Dystrophies constitutionelles": Chlorosis, leukemia, scorbutus and purpura, scrofula, Addison's disease and diabetes.

Niemeyer made almost the same grouping in his textbook, and as late as 1902 we find Strümpell calling these affections of the blood and of the metabolism, constitutional diseases.

As already remarked, however, the renewed interest in the problem of predisposition as well as the modern research on heredity caused "constitution" again to be discussed in its old sense as relating to purely personal properties. The general interest in constitutional pathology in this sense has been aroused chiefly by the two German clinicians, Martius and Kraus. Many clinical concepts and facts have been reviewed from this point of view and this has resulted in many additions to clinical knowledge.

If we were to attempt to define or explain the term "constitution" in a way answering to modern views, we should have to call it the nature of the body, including under this all inherent qualities, such as the anatomical structure of the body, its morphological composition, as well as the functioning properties of the separate organs and cells. A constitutional anomaly is, in consequence, a divergence from the normal in build or functional capacity of the organism, either in its entirety or in its separate parts.

No one knows better than the physician that human beings are not "born alike," but already at birth differ in "constitution," both as regards build and organic functions. As is generally recognized, there is no hard and fast line between the normal and the abnormal, but medically speaking one would be inclined to demand a certain unfitness, a lowering of the efficiency of the individual or organ concerned in order to speak of a constitutional anomaly, a constitutional disease.

Such constitutional anomalies are often due to hereditary disposition, but they may also be acquired, before or after birth. In both cases they are characterized by morbid changes, as a rule permanent, in the nature of the body.

Hitherto, it has proved very difficult to decide where to draw the line concerning constitutional anomalies, and the leading authors in this field, such as Martius, Kraus, Tandler and others, are by no means agreed on this point.

There exists little difference of opinion concerning certain purely local anomalies, either the anatomical ones, such as congenital deformities, or the functional ones, such as color blindness and other analogous affections of individual organs. But the liveliest discussion has arisen in regard to the more general constitutional anomalies which also are characterized both by anatomical and functional disturbances and demand for their recognition methods for both anatomical and functional diagnosis.

The first step towards the anatomical diagnosis of these conditions was made by Beneke in 1878. He made an extensive series of measurements of the size of the various organs post mortem, and by comparing these measurements he sought to obtain a method for estimating their degree of functional power. This attempt, however, did not lead to any practical results.

The study of status thymico-lymphaticus, described by Paltauf in 1889, led to results of greater importance in this connection. By anatomical studies of this condition the persistence of the thymus gland and hyperplasia of the lymphatic tissues was demonstrated. It was proved that these anatomical conditions predispose to sudden death under circumstances where this would otherwise not have been expected. Special studies of importance in this connection have consisted in the investigation of the variations in bodily habitus of different individuals. The study was inaugurated by the Frenchman, Tuffier (1894) and especially by the Austrian, Stiller (1896). As one of the results of this study, the latter described what he called the asthenic constitutional disease. This method of study has been further developed by Kraus and his disciples at the Charité in Berlin. Kraus and his disciples have sought to establish what Kraus calls "an anthropological clinic" in which the methods of of anthropology have been employed in measuring and investigating the build of various individuals and in investigating deviations from the normal. Interest has centered chiefly in the too narrowly built chest, which according to these investigators is the chief cause of a series of alterations in the thoracic and abdominal organs, or at any rate, is their constant concomitant. For instance, this type of chest is said to be accompanied by a deficient development of the heart and the great vessels, and is frequently associated with a long vertically placed stomach (gastroptosis), a high and narrow liver, movable kidneys, etc. These organic deformities are further said to involve a great liability to functional disturbance in the organs concerned. Narrow-chested men with a comparatively small heart have not been able to stand the almost superhuman strain of the world war, but have contracted cardiac incompetence under circumstances where strongly built men have not been affected. Individuals suffering from gastroptosis are said to be predisposed to all sorts of dyspepsia and to atony of the stomach. The nervous system of these individuals is believed to be particularly susceptible to harmful agencies so that they are easily exhausted, in brief, that these individuals are neurasthenic.

What unites the various morbid states and symptoms in this instance is the habitus of the patient, the narrow chest, i.e., an anatomical factor, but the chief interest in this study lies in the fact that it reveals or renders probable a functional weakening, a reduction of power, of the misplaced or deformed organs.

In another series of general constitutional anomalies, on the other hand, characteristic functional disturbances alone are present. This is the case in what has been called diathesis; uric acid diathesis, for instance.

In all these general constitutional affections the important fact is that the functional powers of the individual, or of his various organs, are reduced. In the face of any task, insufficiency of the organs will occur more quickly than in normal individuals. The chief importance of these conditions for the individual, and indirectly for the physician, lies, therefore, in their concomitant states, in the fact that they predispose to other diseases. We may say, with Martius, that they denote a premorbid phase. While, through the functional diagnostic methods of Rosenbach, it was attempted to diagnose a morbid state at its inception, it is the aim of constitutional pathology to determine in any individual the disease which may, with probability, be expected to develop.

There is, however, as has recently been pointed out by Siemens, an essential difference between a predisposition to disease and a constitutional anomaly. The latter is a more autonomic concept. It involves a reduction in the power to resist external injurious influences and so predisposes to disease, but so do other conditions which have nothing to do with constitutional anomalies. Typhoid fever, for instance, predisposes to decubitus, diabetes predisposes to furunculosis and to tuberculosis of the lungs, but both typhoid fever and diabetes are well-marked clinical concepts, unrelated to constitutional diseases. However, the various constitutional anomalies are also clinical concepts, clinical entities arrived at like other clinical concepts, by means of anatomical or functional diagnosis. They differ, however, from other diseases, by being stable, permanent deviations from the normal; they are not pathological abnormalities existing only for a period of limited duration, they remain with the individual throughout life.

And now the question naturally suggests itself, In what relation do all these constitutional anomalies stand to heredity and to the above-mentioned hereditary diseases?

In reality, all hereditary diseases must be considered as constitutional anomalies. It has even been attempted (by Tandler, Bauer and several others) to restrict the designation "constitutional affection" exclusively to hereditary affections, and to designate as "conditional" all other diseases which do not originate in the germ cells. This attempt, however, meets with many difficulties. A constitutional anomaly, a constitutional disease, in the modern sense, may readily arise, and very often has arisen after birth under the influence of certain external conditions without having been, as it were, "predetermined" in the germ cells. This, for instance, seems to be the rule in the case of certain of the anomalies of development, such as the narrow chest. As a matter of fact, the constitutional anomalies as well as the predispositions and immunities may be either inherited or acquired.

This whole chapter of clinical medicine, however, is still in a state of evolution and consequently is still somewhat obscure and confused. Nevertheless, owing to the interest which has been aroused in this subject, many new points of view have been developed, and new methods for estimating the state of health and power of resistance to injurious influences of each separate individual have been devised. In its relation to the subject of nosography this movement has a special interest; in the first place, because it has already enriched nosography with a new series of morbid categories and pictures and gives promise of still further additions, and in the second place, because it has brought to our consciousness the relativity of our nosographical concepts and the difficulties of a sharply delimited classification of diseases. It has thus brought support for the views of the many authors who have maintained throughout the century the artificiality of every fixed classification of diseases.

Every morbid phenomenon, according to constitutional pathology, is the result of an injurious morbific factor in conjunction with a susceptibility of the organism. This susceptibility is most closely associated with the whole constitution of the individual, his anatomical and physiological nature. The latter, again, is influenced partly by hereditary predisposition, partly by the conditions under which the organism has developed. Hence the ultimate phenomenon is so complex that in each case of disease it can only be understood by an analytical study of all the factors concerned. Not only must the morbific cause be investigated, but also the inherited as well as the acquired constitution of the patient, as it is exhibited in his habitus of body and in the functional capacity of each separate organ.

In one case the external morbific cause is the entirely dominating factor, as for instance in the influenza which attacks everybody; in another instance, it is the internal morbific cause which governs the etiology, as in the absolutely hereditary bleeding disease, and in still other cases, an indefinable mixture of endogenous and exogenous causes is operative. How then is it possible to maintain, as the goal to which we should aspire, the classification of all morbid phenomena on the basis of etiology? This, as we know, was the goal we had previously set ourselves in nosography.

No guide to the solution of this problem is found in the concepts of phenotype and genotype. All morbid phenomena are components of a phenotype and they are all ultimately a result of the effect of external conditions on the inherent qualities.

As a guide we must determine the cause which specially characterizes the course of a given disease and regard this as the chief cause and employ it as a basis of classification. The morbid phenomena of a case of pneumonia, or of a case of tuberculosis of the lung, are primarily characterized by the special microbe which is present, no matter whether the patient be much or little predisposed to the disease by his constitution. On the other hand, the characterizing feature of a case of myoclonus-epilepsy, or of night-blindness, or of Friedreich's tabes, is its hereditary character, even though external conditions may possibly hasten or sometimes perhaps even prevent the appearance of the disease. The cause which in each case gives the disease its clinical character and determines the development and course of the symptoms is then also the one which we should call the actual cause of the disease.

We must, however, once more emphasize that all concepts of disease, like all other concepts denoting species, are human abstractions, not objective entities. Philosophically speaking, everything is fluent; but to the physician who is to live and act in the world, it is necessary to have definite categories of disease to serve as guides and tools.

FINAL REMARKS

On surveying in retrospect the evolution of nosography over the period here dealt with, it is not difficult to gain a comprehensive view of its various phases. For centuries physicians were restricted to the direct observation of symptoms. This only led to the description of some conspicuous symptoms and symptom-complexes. Ingenious observers now and then established clinical pictures of more lasting value, but all scientific method of classification was lacking. Sydenham, past-master in the art of observation, soon felt the need of some method by which to describe the diseases. As we have seen, he discovered such a method applicable to a limited field through the study of the seasonal occurrence of the epidemics. With this exception it was exclusively by the study of the regular combination of symptoms and by the observations of the course of the symptoms that he and the succeeding clinicians had to proceed.

Then, pathological anatomy stepped in with physical diagnosis established on Laënnec's stethoscopy, and this movement dominated the first half of the nineteenth century. Next, physiology gradually developed with the study of function, and growing out of this, functional diagnosis became a new basis for nosography. But both the anatomical and the physiological methods of research became effective only when they were applied in conjunction with, and under the guidance of, direct clinical observation of the characterisitic development and course of the diseases. Only then were they able to advance nosography as it was desired.

Much surer and more striking progress in the delimitation and description of diseases was attained through the application of bacteriological methods. Through the latter the very essence of the disease was revealed, and it became apparent that the classification of morbid phenomena, their grouping in species and genera, which at all times had been attempted, was in reality analogous to referring definite physical phenomena to definite causes. It was only when this had been recognized and this train of reasoning with all its resulting demands and tendencies adopted, that clinical research—diagnosis, anatomical and functional—was supplied with a unity of aim. Only then did concerted efforts with various methods succeed in supplying a solid foundation for the further development of nosography. This point of view has also been of assistance in the application of the knowledge concerning heredity to medical nosology.

Of course, the purely anatomical clinical pictures, such as pleurisy, spinal tumor, etc., will always retain their full value, as likewise those which are purely functional, such as hemiplegia, gastric achylia, auricular fibrillation; but only when we have penetrated to the underlying causes, and described the etiological entities of disease, will the goal of nosography have been reached.

The attempt to "describe the diseases" borrowed from descriptive natural history has been found to be inseparably bound up with the quest for the causes of the morbid phenomena. Clinical medicine is, therefore, at work, like the other natural sciences, but following its own particular methods, at the great task of attempting to understand natural phenomena in order to be able to control them.

The nosographical method of research is, above all, analytical. Analysis of data obtained by mere observation of patients, however, no longer suffices. The clinic aims at the most profound analysis of the morbid phenomena that is possible, with all available methods of examination—physical, chemical, physiological and morphological, and in addition, it employs the clinical experiment in order to measure the degree of functional disorder by means of functional tests. It does not stop short at this, however, but goes on to construct by synthesis, clinical pictures of individual diseases subject to fixed laws in their course and development. Speaking figuratively, these clinical pictures of disease may very well be called species, but, as already remarked, they really denote a delimited group of natural phenomena produced by some definite cause.

Every time any important advance is made in this field it is considered in the clinic to be a great feat, and the description of a new disease is of extremely great importance in practical medicine. To the physiologist and the worker in the laboratory, morbid categories are subordinate concepts, but to the physician, to the clinician, the reverse is the case; he cannot live, cannot speak, cannot act without them.

The ultimate aim of the clinic is not, of course, the development of nosology, the naming of a morbid condition, or the referring of an example to a given category. Classification of disease will always be changing and will never be fixed until we know all the various factors which are concerned in producing the morbid phenomena, the external causes as well as the inherited or acquired constitution, and understand how they interact with each other. The final aim of medicine is to acquire a knowledge concerning etiology and concerning the consequent development of the morbid process so as to be able to adopt the right line of action. Nosography is one of the means to this end; it is one of the working methods employed by the clinic for the recognition and understanding of the phenomena and their relations. As we have seen, it has proved a very fruitful working method up to our own day, and the greatest names in clinical medicine are found among its followers.

The important advances in this field, however, are only exceptionally due to any one man; as a rule, a great number of clinical observers from the various centers of study share in the revelation of new knowledge, and even general practitioners often make important contributions. Experience shows, however, that where the greatest progress is being made in theoretical medicine, there, also, are clinical discoveries most easily made. This serves as additional evidence indicating the intimate connection between the several branches of medical science. Every significant advance in our understanding of pathological processes and functional disturbances will always serve as a strong impulse to the clinic; and we have endeavored to show to how great an extent this is illustrated by the history of nosography. On the other hand, the clinic is a kind of touchstone for testing the value of new theoretical discoveries. The deeper the new views go, the more surely will they set their mark on the clinic, and especially on nosography and classification.

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